STUDY OF ANTIDIABETIC ACTIVITY ON *AVERRHOA CARAMBOLA* LEAVES

Project Proposal submitted to

The Tamil Nadu Dr.M.G.R Medical University Chennai

In partial fulfillment of the degree of

MASTER OF PHARMACY

(Pharmacology)

Submitted by

MUHAMED SHANOOF N.P

(Reg No :261526159)

Under the guidance of

Dr. C. SENTHIL KUMAR, M.Pharm., Ph.D

Associated Professor
Department of Pharmacology
Karpagam College of Pharmacy
Coimbatore-32

SEPTEMBER 2017

DEPARTMENT OF PHARMACOLOGY

KARPAGAM COLLEGE OF PHARMACY

COIMBATORE-641 032

CERTIFICATE

This is to certify that this dissertation entitled **"STUDY OF ANTIDIABETIC ACTIVITY ON *AVERRHOA CARAMBOLA* LEAVES"** Submitted by **Mr. MUHAMED SHANOOF N.P** to The Tamil Nadu Dr.M.G.R Medical University, Chennai in partial fulfilment for the degree of **Master of Pharmacy in Pharmacology** is a bonafied work carried out by the candidate under the guidance and supervision of Dr.C. Senthil Kumar M.Pharm., Ph.D in the Department of Pharmacology, Karpagam College of Pharmacy Coimbatore-32.

I have fully satisfied with his performance and work. I have forward this dissertation work for evaluation.

Place :

Date :

Dr. S. MOHAN M.Pharm., Ph.D.,

Principal

CERTIFICATE

This is to certify that this dissertation entitled **"STUDY OF ANTIDIABETIC ACTIVITY ON *AVERRHOA CARAMBOLA* LEAVES"** Submitted by **Mr. MUHAMED SHANOOF N.P** to The Tamil Nadu Dr.M.G.R Medical University, Chennai in partial fulfilment for the degree of **Master of Pharmacy in Pharmacology** is a bonafied work carried out by the candidate under the guidance and supervision of Dr .C. Senthil Kumar M.Pharm., Ph.D in the Department of Pharmacology, Karpagam College of Pharmacy Coimbatore-32.

Place :

Date :

Prof.G. NAGARAJAPERUMAL

Head of the Department

Department of Pharmacology

CERTIFICATE

This is to certify that this dissertation entitled entitled **"STUDY OF ANTIDIABETIC ACTIVITY ON *AVERRHOA CARAMBOLA* LEAVES"** submitted by **Mr. MUHAMED SHANOOF N.P** to The Tamil Nadu Dr.M.G.R Medical University, Chennai in partial fulfilment for the degree of **Master of Pharmacy in Pharmacology** is a bonafied work carried out under my guidance and supervision in the Department of Pharmacology, Karpagam College of Pharmacy Coimbatore-32.

Place:

Date :

Dr. C. SENTHIL KUMAR, M.Pharm., Ph.,D

Associate Professor

Karpagam College of Pharmacy

CERTIFICATE

This is to certify that this dissertation entitled **"STUDY OF ANTIDIABETIC ACTIVITY ON *AVERRHOA CARAMBOLA* LEAVES"** submitted by **Mr. MUHAMED SHANOOF N.P** to the Tamil Nadu Dr. M.G.R Medical University, Chennai in partial fulfilment for the degree of **Master of Pharmacy in Pharmacology** is a bonafied work carried out by the candidate under my guidance at **SURAS LABORATORIES,** during the academic year 2016-2017.

Place :

Date :

Dr. P. Krantikumar

Co-guide

DECLARATION

I hereby declare that this dissertation entitled **"STUDY OF ANTIDIABETIC ACTIVITY ON *AVERRHOA CARAMBOLA* LEAVES"** submitted by me, in partial fulfilment of the requirements for the degree of **Master of Pharmacy in Pharmacology** to The Tamil Nadu Dr. M.G.R Medical university, Chennai is the result of my original and independent research work carried out under the guidance of **Dr. C. SENTHIL KUMAR M.Pharm.,Ph.D** Associate Professor, Department of Pharmacology, Karpagam College of Pharmacy, Coimbatore-32, & Co-Guide **Dr. P. KRANTIKUMAR, Suras Laboratories,** during the academic year 2016- 2017.

Place : **Mr. MUHAMED SHANOOF N.P**

Date:

EVALUATION CERTIFICATE

This is to certify that the dissertation work **"STUDY OF ANTIDIABETIC ACTIVITY ON AVERRHOA CARAMBOLA LEAVES"** submitted by, **Mr. SHANOOF N.P** bearing Reg.No**: 261526159** to The Tamil Nadu Dr. M. G. R Medical University, Chennai in partial fulfilment for the Degree of **Master of Pharmacy in Pharmacology** is a bonafied work carried out during the academic year 2016-2017 by the candidate at Department of Pharmacology, Karpagam College of Pharmacy, Coimbatore and was evaluated by us.

Examination centre:

Date:

Internal Examiner

Convener of Examination

External examiner

ACKNOWLEDGEMENT

At first I bow to my **GOD**, who inspires for the beginning and completion of every effort for a good work. I hereby take this opportunity to acknowledge all those who have helped us in the completion of this dissertation work**.**

We express our extended thanks to our most respected Chairman and respected trustee **Dr.R.Vasanthakumar,** Karpagam Educational Trust, for the facilities provided to carry out this project.

My sincere thanks to our respected and beloved Principal **Dr. S. MOHAN**, **M. Pharm, Ph.D.**, Karpagam College of Pharmacy for his encouragement and also providing all facilities in this institutions to the fullest possible extent enabling me to complete this work successfully.

It is my pleasure to express my honorable thanks to **Prof. G. NAGARAJAPERUMAL, M. Pharm,** Professor & Head, Deportment of Pharmacology, Karpagam College of Pharmacy.who helped us carried out the validation and degradation studies related to our project.

I would like to take this opportunity in expressing my deep sense of gratitude to my beloved guide **Dr. C. SENTHIL KUMAR M. Pharm., Ph.D** Associate Professor, Department of Pharmacology, Karpagam College of Pharmacy under whose active guidance, Innovative ideas, constant inspiration and encouragement of the work entitled, **"STUDY OF ANTIDIABETIC ACTIVITY ON AVERRHOA CARAMBOLA LEAVES"** has been carried out.

I convey my gratitude to **Dr. V. E. IDACHRISTI, M. Pharm, Ph.D.**, Professor & Head Department of Pharmacognosy, Helped me to proceed useful ideas.

I am also convey my thanks to **Dr. M. KARPAGAVALLI, M. Pharm, Ph.D.**, Professor & Head Department of Pharmaceutical Chemistry, for encouragement and valuable suggestion during this work.

It is my pleasure to express my honorable thanks to **Dr. S. JANARDHANAN, M. Pharm.**, Ph.D., Professor Department of Pharmacognosy, helped me to proceed project work.

It is my pleasure to express my honorable thanks to **Mr. A. MUTHUKUMAR, M. Pharm**, Asst. Professor, Department of Pharmacology, helped me to proceed project work.

My whole hearted thanks to **Mr. D. RANJITH KUMAR, M. Pharm,** Asst. Professor, Department of Pharmaceutical Analysis for his kind advice.

I convey my gratitude to **Mrs. MARY PRIYA**, **M. Pharm**. Asst. Professor Department of Pharmacy Practice, Helped me to given useful ideas.

I convey my thanks to **Ms M. SATHYA.**, Lab Assistant, Department of Pharmacology for his kind support.

I express my sincere thanks to **Mr. K. SIMON**, Lab Assistant, Department of Pharmaceutical Chemistry for his kind support.

I convey my gratitude thanks to **Mr. S. ANTONY DAS**, Lab Assistant, Department of Pharmaceutics for his kind support.

I am duly bound to all my nonteaching staffs of Karpagam College of Pharmacy for their valuable and co operation

Mr. MUHAMED SHANOOF N.P

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBRIVATION

S.No	Short form	Full form
1	OGTT	Oral glucose tolerance test
2	WHO	World health organisation
3	CE	Conformity European
4	NPH	Natural protamine hagedorn
5	IDF	Intermediate distribution frame
6	HBA1C	Haemoglobin although one chemical
7	ACELs	Angiotensin converting enzyme inhibitors
8	ARBs	Angiotensin receptor blockers
9	HDL	High density lipoprotein
10	A1C	Although one chemical
11	AA	Antioxidant activity
12	TFC	Total flavonoid content
13	TPC	Total phenolic content
14	DPPH	-2,2-di phenyl-1-picrylhydrazyl
15	BCB	-β carotene bleaching
16	FRAP	Ferric reducing antioxidant power
17	EC50	Effective concentration
18	TE/g	Totally enclosed
19	SEM	Scanning electron microscope
20	ANOVA	Analysis of variance
21	IC50	Inhibitory concentration
22	HELAC	Hydro alcoholic extract of leaves of averrhoa carambola
23	C^{14}	Carbon
24	MPO	Myeloperoxidase

25	ID50	Infection dose
26	HCC	Hepatocellular carcinoma
27	DENA	Diethyl nitrosamine
28	ACE	Angiotensin converting enzyme
29	CCL4	Carbon tetra chloride
30	HCL	Hydrochloride
31	OECD	Organisation for economic cooperation and development
32	LD50	Lethal dose
33	OAEC	Organisation of animal ethics committee
34	CMC	Carboxy methyl cellulose
35	PO	Per oral
36	IP	Intra peritoneal

1. INTRODUCTION

Diabetes mellitus (DM) is a collection of metabolic issue described by hyperglycemia; is related with variations from the normal sugar, fat and protein digestion; and results in incessant intricacies including microvascular, macrovascular, and neuropathic disorders[1]. It is in recent times evaluated that no less than 171 million individuals worldwide have diabetes, and this figure is probably going to dramatically increase by 2030. Additionally, around 3.2 million passings consistently are owing to difficulties of diabetes; six passings each minute. Aside from presently accessible helpful alternatives like insulin, sulfonylureas, biguanides, thiazolidinediones etc, numerous home grown drugs have been prescribed for the treatment of diabetes because of their lesser symptoms and expanded agreeableness. Presently a day, there are various plants which are known for their antidiabetic potential. All through the world numerous conventional plant medicines for diabetes exist[2]. Nonetheless, few have gotten logical or medicinal investigation and the WHO has suggested that conventional plant medications for diabetes warrant facilitate evaluation.

Indian physicians around the same time identified the disease and classified it as Madhumeha or "honey urine", noting but the urine would attract ants. This is possibly due to the diet and life-style of the ancient people, or because the clinical symptoms were observed during the advanced stage of the disease. Galen named the disease "Diarrhea of the urine" (diarrhea urinosa). The earliest surviving work with a detailed reference to diabetes is that of Aretaeus of Cappadocia (2nd or early 3rd century CE). Type 1 and type 2 diabetes were identified as separate conditions for the first time by the Indian physicians Sushruta and Charaka in 400-500 CE with type 1 associated with youth and type 2 with being overweight. Effective treatment was not developed until the early part of the 20th century, when Canadians Frederick Banting and Charles Herbert Best isolated and purified insulin in 1921 and 1922. This was followed by the development of the long-acting insulin NPH in the 1940s. Medicinal plants constitute an important natural wealth of a country. They play a significant role in providing primary health care services to the rural population. They serve as therapeutic agents as well as important raw materials for the

manufacture of traditional medicines. Ethno pharmacology is the study of plants used in traditional medicine and is therefore heavily reliant on interactions between researchers and indigenous communities who passed on the traditional knowledge over generations. Whilst in the main, ethno pharmacology focuses on the presence or absence of evidence for specific therapeutic responses through the use of herbal remedies, the field also extends into phytochemistry where the aim is to identify the chemical constituent of the plant or plant extract that is responsible for the pharmacological activities inherent to a specific plant.

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter. WHO has listed 21,000 plants, which are used for medicinal purposes around the world. Therefore, with the rising number of diseases lately, many researchers have evaluated the medicinal plants as alternative therapeutic agents. The effectiveness and safety of drugs derived from medicinal plants require scientific evaluation to establish the profiles of therapeutic effectiveness and toxicity of plant products. One example of such products is antihyperglycemic agents for use in the treatment of diabetes mellitus.

Importance of medicinal plants and traditional medicines

Medicinal plants, since time immemorial, have been used in virtually all cultures as a source of medicine. It has been estimated that about 80-85% of population both in developed and developing countries rely on traditional medicine for their primarily health care needs and it is assumed that a major part of traditional therapy involves the use of plant extracts or their active principles. Due to lack of organized health care systems in developing countries like Ethiopia, people with chronic diseases like diabetes are among the worst suffers in their communities today. Hence, most of the populations still have limited access or no access, especially those in remote areas, to modern medicines. Instead they use traditional medicines for a range of diabetic complications.

Diabetes mellitus

Diabetes mellitus is described as metabolic disorder which resulting from defects in insulin secretion or insulin action or both diabetes mellitus could cause long-term damage, dysfunction and failure in many organs. Patients with diabetes can develop heart disease, kidney disease, and blindness, vascular or neurological problems that can lead to amputation and can suffer increased rates of mortality. Moreover, the death rate in patients with diabetes is much higher than in persons without the disease. According to the estimation of the International Diabetes Federation (IDF), one among ten adults would have diabetes by 2030. There were 366 million people having diabetes in 2011; this will increase to 552 million people by 2030.

The number of people got type 2 diabetes is increasing every year and many people remain un-diagnostic. In the demand of preventing and treating Diabetes Mellitus, there are many synthetic drugs have been researched and developed such as Sulphonylureas, thiazolidinediones, Glinide, Metformin. However, they are not optimum solution especially for developing country like Vietnam. They retain many side effects and relatively expensive. There is a need to investigate herbal drug based medicine, which has available resources, easy to use, cheap and less side effects.

Classification of diabetes mellitus

Type I diabetes: Insulin-dependent or childhood-onset, is characterized by a lack of insulin production.

Type II diabetes: Non-insulin-dependent or maturity/adult-onset diabetes.

Type III or Gestational diabetes: This type of diabetes first occurs during pregnancy.

Secondary diabetes: Diabetes may develop as a consequence of other diseases or medication**.**

Prevalence and incidence of diabetes mellitus

Globally, the prevalence of diabetes, without type distinction, was estimated to be 4% in 1995. According to WHO, it is estimated that 3% of the world's population have diabetes and the prevalence is expected to double by the year 2025 to 6.3%. There will be a 42% increase from 51 to 72 million in the developed countries and 170% increase from 84 to

228 million, in the developing countries. Thus, by the year 2025, over 75% of all people with diabetes will be in the developing countries, as compared to 62% in 1995.

Medicinal plants constitute an important natural wealth of a country. They play a significant role in providing primary health care services to the rural population. They serve as therapeutic agents as well as important raw materials for the manufacture of traditional medicines. Ethnopharmacology is the study of plants used in traditional medicine and is therefore heavily reliant on interactions between researchers and indigenous communities who passed on the traditional knowledge over generations. Whilst in the main, ethnopharmacology focuses on the presence or absence of evidence for specific therapeutic responses through the use of herbal remedies, the field also extends into phytochemistry where the aim is to identify the chemical constituent of the plant or plant extract that is responsible for the pharmacological activities inherent to a specific plant.

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter. WHO has listed 21,000 plants, which are used for medicinal purposes around the world. Therefore, with the rising number of diseases lately, many researchers have evaluated the medicinal plants as alternative therapeutic agents. The effectiveness and safety of drugs derived from medicinal plants require scientific evaluation to establish the profiles of therapeutic effectiveness and toxicity of plant products. One example of such products is antihyperglycemic agents for use in the treatment of diabetes mellitus.

Importance of medicinal plants and traditional medicines

Medicinal plants, since time immemorial, have been used in virtually all cultures as a source of medicine. It has been estimated that about 80-85% of population both in developed and developing countries rely on traditional medicine for their primarily health care needs and it is assumed that a major part of traditional therapy involves the use of plant extracts or their active principles. Due to lack of organized health care systems in

developing countries like Ethiopia, people with chronic diseases like diabetes are among the worst suffers in their communities today. Hence, most of the populations still have limited access or no access, especially those in remote areas, to modern medicines. Instead they use traditional medicines for a range of diabetic complications.

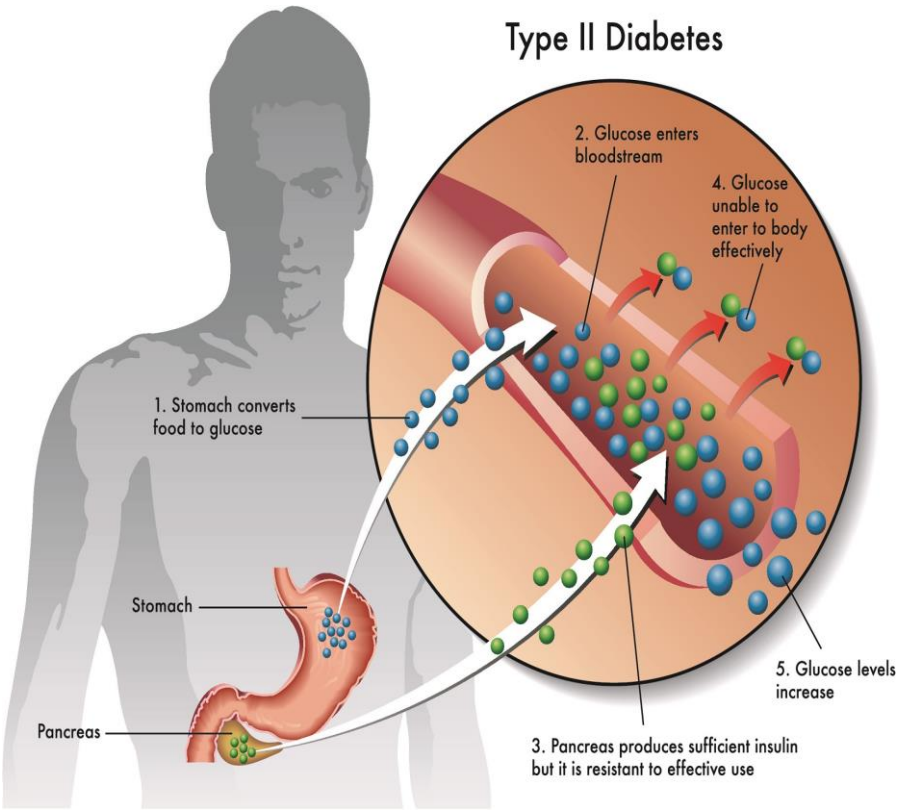


Fig 1. Main Symptoms of Diabetes

Overview of the most significant symptoms of diabetes

The classic symptoms of untreated diabetes are weight loss, polyuria (frequent urination), polydipsia (increased thirst), and polyphagia (increased hunger). Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes.

Several other signs and symptoms can mark the onset of diabetes, although they are not specific to the disease. In addition to the known ones above, they include blurry vision,

headache, fatigue, slow healing of cuts, and itchy skin. Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. A number of skin rashes that can occur in diabetes are collectively known as diabetic dermadromes.

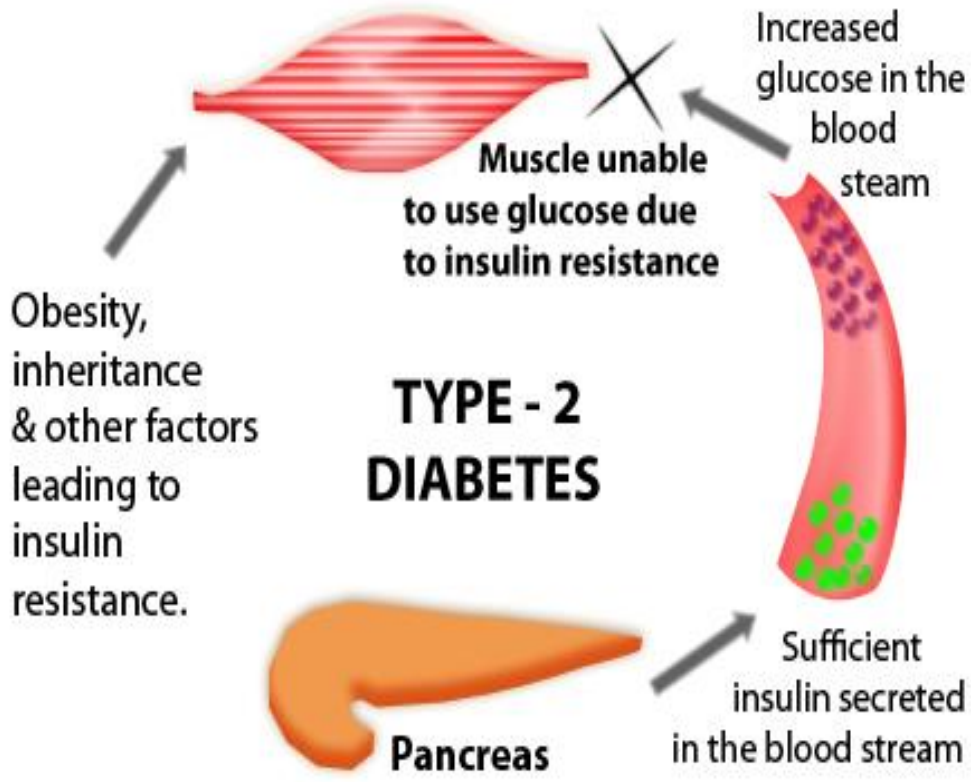


Fig 2. Fate of Type-II diabetes

People (usually with type 1 diabetes) may also experience episodes of diabetic ketoacidosis, a type of metabolic problems characterized by nausea, vomiting and abdominal pain, the smell of acetone on the breath, deep breathing known as Kussmaul breathing, and in severe cases a decreased level of consciousness.

A rare but equally severe possibility is hyperosmolar nonketotic state, which is more common in type 2 diabetes and is mainly the result of dehydration.

Complications

All forms of diabetes increase the risk of long-term complications. These typically develop after many years (10–20), but may be the first symptom in those who have otherwise not received a diagnosis before that time.

The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease and about 75% of deaths in diabetics are due to coronary artery disease. Other "macrovascular" diseases are stroke, and peripheral vascular disease.

The primary microvascular complications of diabetes include damage to the eyes, kidneys, and nerves. Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina of the eye, and can result in gradual vision loss and potentially blindness. Damage to the kidneys, known asdiabetic nephropathy, can lead to tissue scarring, urine protein loss, and eventually chronic kidney disease, sometimes requiring dialysis or kidney transplant. Damage to the nerves of the body, known as diabetic neuropathy, is the most common complication of diabetes. The symptoms can include numbness, tingling, pain, and altered pain sensation, which can lead to damage to the skin. Diabetes-related foot problems (such as diabetic foot ulcers) may occur, and can be difficult to treat, occasionally requiring amputation. Additionally, proximal diabetic neuropathy causes painful muscle wasting and weakness.

There is a link between cognitive deficit and diabetes. Compared to those without diabetes, those with the disease have a 1.2 to 1.5-fold greater rate of decline in cognitive function.

Diagnosis

Diabetes mellitus is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating any one of the following:

- Fasting plasma glucose level ≥ 7.0 mmol/l (126 mg/dl)
- Plasma glucose ≥ 11.1 mmol/l (200 mg/dl) two hours after a 75 g oral glucose load as in a glucose tolerance test

- Symptoms of hyperglycemia and casual plasma glucose ≥ 11.1 mmol/l (200 mg/dl)
- Glycated hemoglobin (Hb A1C) ≥ 6.5%.

A positive result, in the absence of unequivocal hyperglycemia, should be confirmed by a repeat of any of the above methods on a different day. It is preferable to measure a fasting glucose level because of the ease of measurement and the considerable time commitment of formal glucose tolerance testing, which takes two hours to complete and offers no prognostic advantage over the fasting test. According to the current definition, two fasting glucose measurements above 126 mg/dl (7.0 mmol/l) is considered diagnostic for diabetes mellitus.

Per the World Health Organization people with fasting glucose levels from 6.1 to 6.9 mmol/l (110 to 125 mg/dl) are considered to have impaired fasting glucose. People with plasma glucose at or above 7.8 mmol/l (140 mg/dl), but not over 11.1 mmol/l (200 mg/dl), two hours after a 75 g oral glucose load are considered to haveimpaired glucose tolerance. Of these two prediabetic states, the latter in particular is a major risk factor for progression to full-blown diabetes mellitus, as well as cardiovascular disease. The American Diabetes Association since 2003 uses a slightly different range for impaired fasting glucose of 5.6 to 6.9 mmol/l (100 to 125 mg/dl).

Glycated hemoglobin is better than fasting glucose for determining risks of cardiovascular disease and death from any cause.

The rare disease diabetes insipidus has similar symptoms to diabetes mellitus, but without disturbances in the sugar metabolism (*insipidus* means "without taste" in Latin) and does not involve the same disease mechanisms.

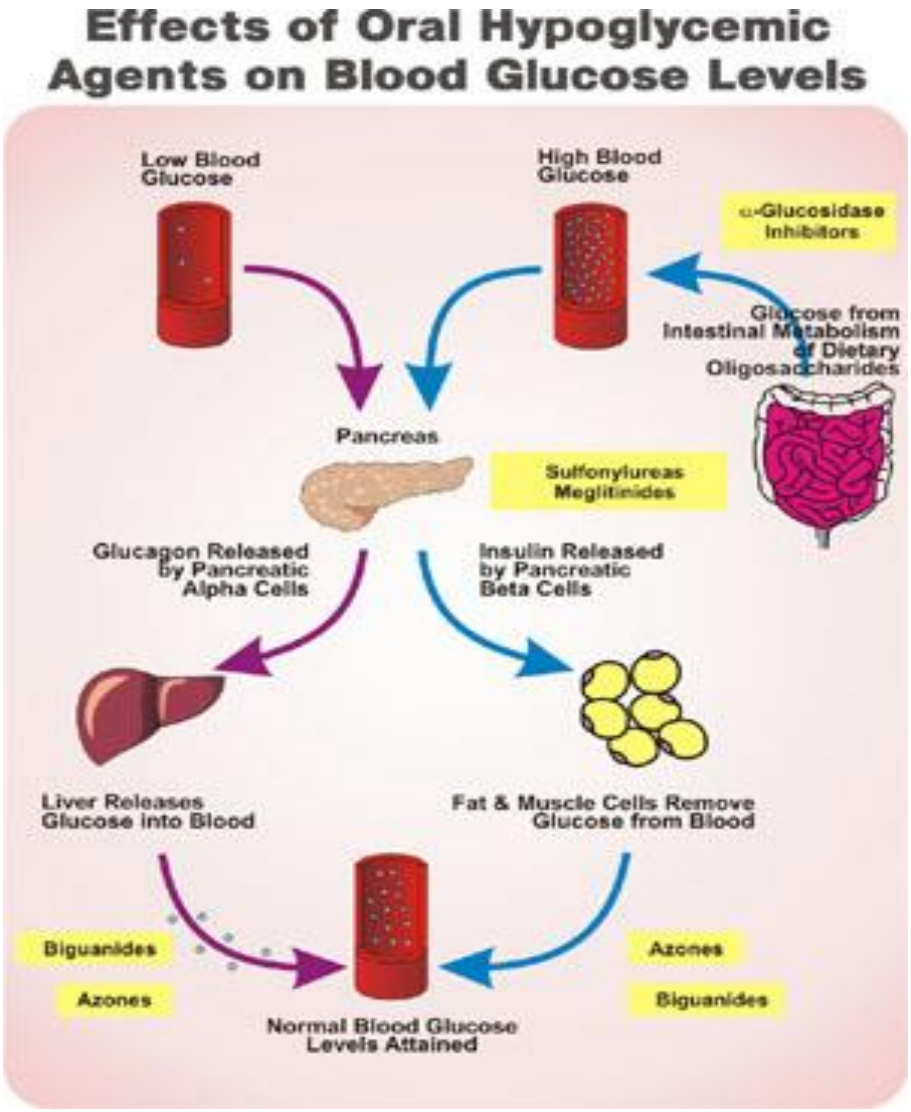


Fig 3. Oral antidiabetic agents site of action

WHO DIABETES DETAILS			
Condition	**2 hour glucose**	**Fasting glucose**	**HbA_{1c}**
Unit	mmol/l(mg/dl)	mmol/l(mg/dl)	%
Normal	<7.8 (<140)	<6.1 (<110)	<6.0
Impaired fasting glycaemia	<7.8 (<140)	≥ 6.1(≥110) & <7.0(<126)	6.0–6.4
Impaired glucose tolerance	≥7.8 (≥140)	<7.0 (<126)	6.0–6.4
Diabetes mellitus	≥11.1 (≥200)	≥7.0 (≥126)	≥6.5

Table 1. WHO diabetes Information chart

Prevention and Treatment

There is no known preventive measure for type 1 diabetes. Type 2 diabetes can often be prevented by a person being a normal body weight, physical exercise, and following a healthy diet. Dietary changes known to be effective in helping to prevent diabetes include a diet rich in whole grains and fiber, and choosing good fats, such as polyunsaturated fats found in nuts, vegetable oils, and fish. Limiting sugary beverages and eating less red meat and other sources of saturated fat can also help in the prevention of diabetes. Active smoking is also associated with an increased risk of diabetes, so smoking cessation can be an important preventive measure as well.

Diabetes mellitus is a chronic disease, for which there is no known cure except in very specific situations. Management concentrates on keeping blood sugar levels as close to normal ("euglycemia") as possible, without causing hypoglycemia. This can usually be accomplished with diet, exercise, and use of appropriate medications (insulin in the case of type 1 diabetes; oral medications, as well as possibly insulin, in type 2 diabetes).

Learning about the disease and actively participating in the treatment is vital for people with diabetes, since the complications of diabetes are far less common and less severe in people who have well-managed blood sugar levels. The goal of treatment is an HbA1C level of 6.5%, but should not be lower than that, and may be set higher. Attention is also paid to other health problems that may accelerate the deleterious effects of diabetes. These include smoking, elevated cholesterollevels, obesity, high blood pressure, and lack of regular exercise. Specialised footwear is widely used to reduce the risk of ulceration, or re-ulceration, in at-risk diabetic feet.

Lifestyle:

People with diabetes can benefit from education about the disease and treatment, good nutrition to achieve a normal body weight, and sensible exercise, with the goal of keeping both short-term and long-term blood glucose levels within acceptable bounds. In addition, given the associated higher risks of cardiovascular disease, lifestyle modifications are recommended to control blood pressure.

Medications:

Metformin is generally recommended as a first line treatment for type 2 diabetes, as there is good evidence that it decreases mortality. Routine use of aspirin, however, has not been found to improve outcomes in uncomplicated diabetes. Angiotensin converting enzyme inhibitors (ACEIs) improve outcomes in those with DM while the similar medications angiotensin receptor blockers (ARBs) do not.

Type 1 diabetes is typically treated with a combinations of regular and NPH insulin, or synthetic insulin analogs. When insulin is used in type 2 diabetes, a long-acting

formulation is usually added initially, while continuing oral medications. Doses of insulin are then increased to effect.

In those with diabetes some recommend blood pressure levels below 120/80 mmHg; however, evidence only supports less than or equal to somewhere between 140/90 mmHg to 160/100 mmHg.

Class	Approved Drugs	Mechanism of action	Limitations
Sulphonylureas (Insulin secretagogues)	2 (2nd gen) 4 (1st gen)	Act on pancreatic β Cells to release insulin	Insulin resistance
Biguanides (Insulin sensitizers)	Only one (Metformin)	Decrease glucose release by liver improves insulin sensitivity	lactic acidosis
Thiazolidine-diones (Insulin sensitizers)	Only one (Glitazones)	Diminish insulin resistance & improve insulin sensitivity	Fluid retention weight gain hypoglycemia, cannot be used in presence of heart & liver disease
∝Glucosidase inhibitors	2 (Acarbose, Miglitol)	Slow the absorption of carbohydrates	flatulence, diarrhoea, abdominal pain

Table 2. Oral antihyperglycemics

Pancreatic transplantation

A pancreas transplant is occasionally considered for people with type 1 diabetes who have severe complications of their disease, including disease requiring kidney transplantation.

Support:

In countries using a general practitioner system, such as the United Kingdom, care may take place mainly outside hospitals, with hospital-based specialist care used only in case of complications, difficult blood sugar control, or research projects. In other

circumstances, general practitioners and specialists share care in a team approach. Home telehealth support can be an effective management techni

Diets And Exercise Treatment

Making healthy food choices is very important to help keep your blood glucose level under control. People with diabetes don't need to buy or prepare special foods. The foods that are best for someone with diabetes are excellent choices for everyone: foods that are low in fat, salt, and sugar, and high in fiber, such as beans, fruits, vegetables, and whole grains. These foods help you reach and stay at a weight that's good for your body. Regular physical activity is important for people with diabetes. Being physically active has been shown to improve blood glucose levels in older people whose levels are high. Exercise is especially good for people with diabetes because it helps control weight, helps insulin work better to lower blood glucose, is good for your heart and lungs, gives you more energy, Regular physical activity improves insulin resistance and lipid profile (reduction in triglyceride and increase in high-density lipoprotein (HDL)) and lowers blood pressure (although blood pressure will rise during exercise),the metabolic benefits in type 2 diabetes are lost within 3-10 days of stopping regular exercise, physical activity also protects against the development of type 2 diabetes

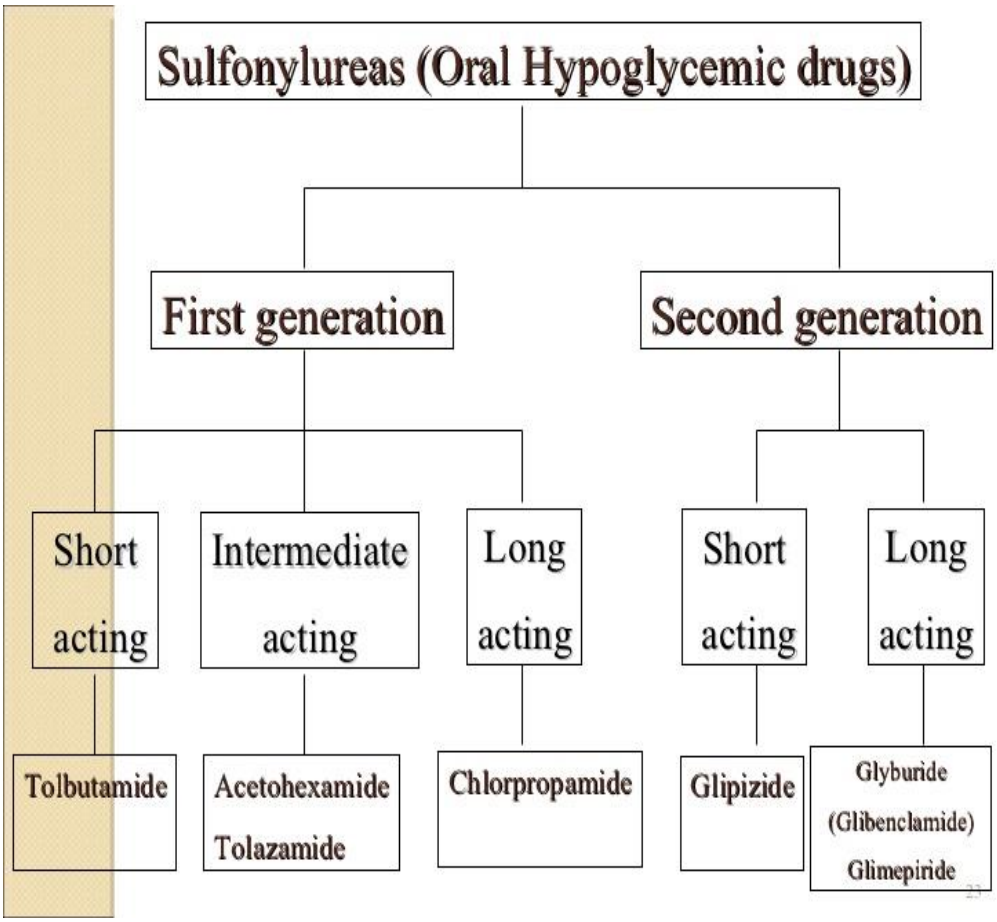


Fig 4. Classification of Sulphonyl Ureas

A1C Test

The A1C test is used to detect type 2 diabetes and prediabetes but is not recommended for diagnosis of type 1 diabetes or gestational diabetes. The A1C test is a blood test that reflects the average of a person's blood glucose levels over the past 3 months and does not show daily fluctuations. The A1C test is more convenient for patients than the traditional glucose tests because it does not require fasting and can be performed at any time of the day.The A1C test result are reported as a percentage. The higher the percentage, the higher a person's blood glucose levels have been. A normal A1C level is below 5.7 percent. An A1C of 5.7 to 6.4 percent indicates prediabetes. People diagnosed with prediabetes may be retested in 1 year. People with an A1C below 5.7 percent may still

be at risk for diabetes, depending on the presence of other characteristics that put them at risk, also known as risk factors. People with an A1C above 6.0 percent should be considered at very high risk of developing diabetes. A level of 6.5 percent or above means a person has diabetes.

Herbal drugs used in the treatment of Diabetes Mellitus

Allopathic medicines are very costly. In contrast, herbal medicines are very cheap. This cost effectiveness makes them all the more alluring. Herbal medicines can be brought without prescription and they are available in all most all health stores. Some herbs can even be grown at home. For certain ailments, herbal medicines are considered to be more effective than allopathic medicines.

Herbal medicines do not have any side effects, as they are free from chemicals. They are also milder than allopathic medicines. The natural detoxification process of the body is effectively enhanced by herbal medicines. They can be used to cleanse the colon, improve digestion and food absorption. Herbal medicines are also very good in boosting the immune system.

Herbal medicines are very effective in curing various digestive disorders like colitis, indigestion, peptic ulcers, and irregular bowel movements. These types of medicines are best for people who are allergic to various types of drugs. Herbal medicines are also effective in boosting the mental health. Most of the ailments related to blood circulation like high blood pressure, varicose ulcers, and many others can be controlled through herbal medicine. Some herbal medicines are very good in reducing the cholesterol level in the blood stream. They are also used to treat coronary artery diseases. Herbal medicine can be used to reduce weight by regulating appetite.

S.No	Botanical name	Family
1.	*Afzelia africana*	Fabaceae
2.	*Amaranthus caudatus*	Amaranthaceae
3.	*Andrographis lineata*	Acanthaceae
4.	*Annona squamosa*	Annonaceae
5.	*Artocarpus heterophyllus*	Moraceae
6.	*Boerhaavia diffusa*	Nyctaginaceae
7.	*Berberis vulgaris*	Berberidaceae
8.	*Brassica juncea*	Brassicaceae
9.	*Caesalpinia bonduc*	Fabaceae
10.	*Caesalpinia digyna*	Caesalpiniaceae
11.	*Cassia glauca*	Caesalpiniaceae
12.	*Cassia siamea*	Fabaceae
13.	*Cleome aspera*	Capparaceae
14.	*Clitoria ternatea*	Fabaceae
15.	*Coccinia indica*	Cucurbitaceae
16.	*Decalepis root*	Asclepiadaceae
17.	*Diospyros peregrina*	Ebenaceae
18.	*Dodonaea viscosa*	Sapindaceae
19.	*Enicostemma littorale*	Gentianaceae
20.	*Eucalyptus globules*	Myrtaceae
21.	*Holarrhena antidysenterica*	Apocynaceae
22.	*Hybanthus enneaspermus*	Violaceae

23.	*Hypericum perforatum*	Hypericaceae
24.	*Lawsonia inermis*	Lythraceae
25.	*Leonotis leonurus*	Lamiaceae
26.	*Litsea coreana*	Lauraceae
27.	*Madhuca longifolia*	Sapotaceae
28.	*Morus rubra*	Moraceae
29.	*Nyctanthes arbor-tristis*	Oleaceae
30.	*Olea europaea*	Oleaceae
31.	*Otostegia persica*	Lamiaceae
32.	*Phlomis persica*	Lamiaceae
33.	*Punica granatum*	Lythraceae
34.	*Rhus coriaria*	Anacardiaceae
35.	*Rosa canina*	Rosaceae
36.	*Salmalia malabarica*	Bombacaceae
37.	*Sansevieria roxburghiana*	Ruscaceae
38.	*Swietenia macrophylla*	Meliaceae
39.	*Symplocos cochinchinensis*	Symplocaceae
40.	*Syzygium cumini*	Myrtaceae
41.	*Tapinanthus bangwensis*	Loranthaceae
42.	*Terminalia bellerica*	Combretaceae
43.	*Terminalia superba*	Combretaceae
44.	*Thespesia populnea*	Malvaceae

Table 3. List of pharmacologically tested anti-diabetic plant materials in steptozotocin induced diabetic animal model

Researchers are wanting to perform antidiabetic considered on ethanolic leaves concentrate of *Averrhoa carambola* having a place with the family Rubiaceae[3,5]. it was acknowledged from the different reports that *Averrhoa carambola* have potential organic exercises, for example, anticancer, hepatoprotective, calming, antifertility, antiamoebic, antinociptive etc. from its different parts. moreover, this plant have additionally utilized as a part of curing different afflictions, for example, ailment, stomach ache, cerebral pain, cool/hack, toothache, fever, agony and swelling, bacterial disease, urinary issues, conjunctivitis, unnatural birth cycle etc. Keeping the perspective of the previously mentioned restorative significance of this plant as my present examination has planned as "Assessment of antidiabetic action of alcoholic concentrates of *Averrhoa carambola* leaves on streptozotocin induced diabetic rats.[6,7,8]

2. LITERATURE REVIEW

1. ***Aktiviti et al 2014.,*** evaluated the Antioxidant Activity (AA), Total Flavonoid Content (TFC), and Total Phenolic Content (TPC) of Oxalidaceae fruit extracts. Two types of Averrhoa carambola L. and two types of bilimbi fruits were used in this study. Bilimbi fruits selected were Averrhoa bilimbi L. and Averrhoa bilimbi cv. while Averrhoa carambola L. selected were Averrhoa carambola L. (honey type) and another type of Averrhoa carambola L. which is known as tart type. The maturity stage for both Averrhoa carambola L. fruits (honey and tart type) were selected at commercial maturity stages which were stage 3 and stage 4. Antioxidant estimation of oxalidaceae fruit extracts were evaluated by using Total Flavonoid Content (TFC) and Total Phenolic Content (TPC), while antioxidant activity were evaluated using scavenging of 2,2-diphenyl-1-picrylhydrazyl radical (DPPH), β- carotene Bleaching (BCB) and Ferric Reducing Antioxidant Power (FRAP) assays. Phytochemical screening of alkaloids, flavonoids, terpenoids, steroids, tannins and saponins were also performed on all samples. Averrhoa carambola L. indicated positive results for all phytochemical screening conducted and similar results were observed from bilimbi fruits, except for alkaloids. Averrhoa carambola L. (tart type) of stage 4 possessed higher TPC and TFC followed by Averrhoa carambola L. (honey type) of stage 4. Averrhoa carambola L. (tart type) of stage 4 also exhibited high scavenging effect (74 %) as determined by DPPH assay with the value of EC50 72.36 mg/ml while Averrhoa carambola L. (honey type) of stage 3 showed significantly lower percentage of scavenging effect. The results also demonstrated that FRAP values of Averrhoa carambola L. (honey type) of stage 4 and Averrhoa carambola L. (tart type) of stage 4 were higher than other samples (5.1023 mmol TE/g and 5.0759 mmol TE/g) and similar trends were observed for β-carotene Bleaching (BCB) assay, where Averrhoa carambola L. (honey type) of stage 4 had the highest value. There were strong positive correlations between antioxidant activity assays and TPC or TFC, hence indicating that the four types of Oxalidaceae fruits used in this study have the potential as natural antioxidant[8].

2. Yin Sze Lim et al., 2013. and Shi Ting Lee Illustrated underutilised tropical fruit that could serves as an alternative food sources to the world. The current study was, therefore, undertaken to investigate the functional potentials of green and ripe star fruits by determining its antioxidant contents and capacities. The antioxidant capacities of star fruit were increased significantly with ripening, except for the total ascorbic acid content. The ripe star fruit peel contained higher total polyphenol (98.19 g TAE/100 g FW), total flavanol (33.31 g CAE/100 g FW) and ascorbic acid contents (1.56 g AAE/100 g FW) than green star fruit peel. Ripe star fruit peel also demonstrated stronger FRAP (1.41 M FEA/100 g FW) and DPPH (75 % inhibition) values than green star fruit peel. The antioxidant capacities of peel were greater than pulp. On the basis of results obtained, the ripe star fruit is a potential source of natural antioxidants owing to its significant antioxidant activities.

3. Suman das et al .,2012.Consumption of diets rich in fruits, vegetables and derived food products can bring substantial health benefits. Research interest thus has increased in natural antioxidants and antimicrobials present in herbs, fruits or vegetables. Underutilized tropical fruits of India provide limitless opportunities for screening of novel drugs. Present study was aimed to understand the antimicrobial and antioxidant activities of tropical fruits Averrhoa carambola Linn. (starfruit) and Zizyphus mauritiana Lam. (jujube) fruits. The edible parts of the fruits were analyzed for different phytochemicals and phenolics, flavonoids, alkaloids and glycosides were found in all ripe and green starfruits or jujubes. Green fruits of Averrhoa carambola showed better antimicrobial activities in comparison with ripe varieties. Widest inhibition zones (14-15 mm DIZ) were seen in cases of extracts of ripe Zizyphus mauritiana against Escherichia coli and Staphylococcus aureus. Common antioxidants like Phenolics, flavonoids and ascorbate were measured. Extracts of ripe fruits contain higher amounts of flavonoids and ascorbate. Bers contain higher amount of ascorbate than starfruits. Ripe jujube or Zizyphus mauritiana extract showed strongest free radical scavenging or antioxidant activity among the tested.

3.Thomas R et al., 2016. Explained Pork nuggets with 'very good' acceptability was processed by incorporating kordoi *(Averrhoa carambola)* fruit juice and bamboo (Bambusa

polymorpha) shoot extract, and their physical, chemical, microbiological and sensorial characteristics were evaluated during 35 days storage under refrigeration. Addition of kordoi fruit juice (4%) and bamboo shoot extract (6%) had a significant effect on the pH, moisture, protein, fat, fiber, instrumental color values and texture profiles of nuggets. Nuggets with juice and extract had significantly lower TBARS values towards the end of the storage period compared to the control. Microbial and sensory qualities of nuggets were significantly improved by the addition of juice and extract. Incorporation of juice and extract at 4% and 6% levels, respectively, increased the storage life of pork nuggets by at least two weeks, i.e. from 21 days to 35 days at 4 ± 1 °C compared to the control.

4.Rupal A et al., 2014. Explained the Consumption of fluoride leads to several physiological disturbances in carbohydrate, lipid and antioxidant metabolisms. *Averrhoa carambola* L. fruit (Star fruit) is a commonly consumed fruit in tropical countries and is an ingredient in folklore medicines. As the fruits have high polyphenolic and antioxidant contents, the present study was undertaken to investigate the potential of star fruit as a dietary supplement in attenuating the fluoride induced hyperglycemia, hypercholesterolemia and oxidative stress in laboratory rats. A four-week exposure to fluoride caused sustained hyperglycemia, hyperlipidemia and oxidative stress and, when the diet was supplemented with star fruit powder, carbohydrate, lipid and antioxidant profiles were restored significantly. It is surmised that the antihyperglycemic, antihypercholesterolemic and antioxidant activities of star fruit in fluoride exposed rats could be due to the presence of polyphenols, flavonoids, saponins, phytosterols, ascorbic acid and fibers in the fruit, which are all well known regulators of carbohydrate, lipid and antioxidant metabolisms. These findings suggest that star fruit can be used as a dietary supplement in fluoride endemic regions to contain fluoride induced hyperglycemia, hyperlipidemia and oxidative stress.

5.Phukan S et al., 2016. Evaluation of the antimicrobial, analgesic and antioxidant activity of ethanolic extract of the leaves of *Averrhoa Carambola*. To test the antimicrobial activity the organisms used were *S. aureus*, *Klebsiella sp, E. coli* and *P. aeruginosa*, *C. albicans*. Zone of inhibitions produced by sensitive organisms were

demarcated by a circular area of clearing around plant extract impregnated discs and were compared with zone of inhibitions of positive controls. Analgesic activity was tested by two methods: acetic acid induced writhing test and Eddy's hot plate mediated pain reaction. The animals were divided into 5 groups: Group I (Normal control), Group II (Standard drug), Group III, IV, V (Ethanolic extract of *A.carrambola* in the doses of 100, 200 and 400mg/kg respectively). To test the antioxidant activity, the mice were divided into 6 groups containing. Paracetamol in the dose of 250mg/kg p.o was administered to all the groups except the first group, which was taken as the normal control, for 10 days to induce oxidative stress. Silymarin in the dose of 25mg/kg p.o was given to the third group as a standard antioxidant. Group IV, V and VI received extract in the dose of 200mg/kg, 400mg/kg and 800mg/kg respectively. Mean ± SEM values were calculated for each group. The data were analyzed using ANOVA and post analysis was done by Dunnett's test. Results were found to be significant ($p<.05$). The results of the present study revealed the antimicrobial, analgesic and antioxidant activity of the leaf ethanolic extract of *A.carrambola.*

6.Sindhu Nettem et al., 2013. Detailed *Averrhoa carambola* of family Oxalidaceae is commonly known as star fruit, carambola and in local name Kamrakh (hindi),Ambanamkaya (telugu). Various parts of tree has been used in traditional folkloric medicine. The present study was concentrated on the in-vitro antioxidant methods like DPPH free radical, nitric oxide radical, hydrogen peroxide radical scavenging and reducing power assays. The ethanolic extract of *Averrhoa carambola* stem was subjected to the above methods. The results of anti oxidant activity revealed that, the ethanolic extract shows good IC50 values. The results were compared with the standard ascorbic acid. The plant contains flavonoids, alkaloids, saponins and tannins. These active constituents alone or in combination may be responsible for the observed antioxidant activity.

7.Edilene et al., 2008. Studied the effect of the oral treatment (20 mg/kg x day) with the hydroalcoholic extract of leaves of *Averrhoa carambola L*. (HELAC) on fasting glycaemia (15 h) was examined. For this purpose, rats that received vehicle (Control group) or HELAC (HELAC group) during 15 days were compared. HELAC group showed

lower fasting glycemia ($p<0.05$). In contrast, livers from HELAC group showed higher ($p<0.05$) glucose production from L-alanine (5 mM). This effect was mediated, at least part of it, by an activation of the catabolism of L-alanine inferred by the increased hepatic urea ($p<0.05$) and L-lactate ($p<0.05$) production. Differently of L-alanine, the glucose production from L-glutamine (5 mM), L-lactate (2 mM) and glycerol (2 mM) was similar (Control group vs. HELAC group). In addition, the HELAC treatment did not change the glucose uptake in soleus muscles, inferred by the incorporation of [^{14}C]-glucose to glycogen (glycogen synthesis) and [^{14}C]-lactate production. Thus, we can conclude that the reduction of fasting glycemia promoted by the treatment with HELAC was not mediated by an inhibition of hepatic gluconeogenesis and/or an increased glucose uptake by muscles.

8.Shejuty Shahreen et al., 2011. Explained and studied *Averrhoa carambola* L. (Oxalidaceae), *Ficus hispida* L.f. (Moraceae), and *Syzygium samarangense*(Blume) Merr. & L.M. Perry (Myrtaceae) are three common plants in Bangladesh, the fruits of which are edible. The leaves and fruits of *A. carambola* and *F. hispida* are used by folk medicinal practitioners for treatment of diabetes, while the leaves of *S. samarangense* are used for treatment of cold, itches, and waist pain. Since scientific studies are absent on the antihyperglycemic effects of the leaves of the three plants, it was the objective of the present study to evaluate the antihyperglycemic potential of methanolic extract of leaves of the plants in oral glucose tolerance tests carried out with glucose-loaded mice. The extracts at different doses were administered one hour prior to glucose administration and blood glucose level was measured after two hours of glucose administration (p.o.) using glucose oxidase method. Significant oral hypoglycaemic activity was found with the extracts of leaves of all three plants tested. The fall in serum glucose levels were dose-dependent for every individual plant, being highest at the highest dose tested of 400 mg extract per kg body weight. At this dose, the extracts of *A. carambola*, *F. hispida*, and *S. samarangense* caused, respectively, 34.1, 22.7, and 59.3% reductions in serum glucose levels when compared to control animals. The standard antihyperglycemic drug, glibenclamide, caused a 57.3% reduction in serum glucose levels versus control. Among the three plants evaluated, the methanolic extract of leaves of *S. samarangense* proved to be the most potent in demonstrating antihyperglycemic effects. The result validates the folk

medicinal uses of *A. carambola* and *F. hispida* in the treatment of diabetes, and indicates that the leaves of *S. samarangense* can also possibly be used for amelioration of diabetes-induced hyperglycemia.

9.Dasgupta et al., 2013. Studied the positive effects of plants on human physiology have enlarged the range of application of medicinal plants. From the centuries, herbal medicines have been used to treat various diseases and now they had become an item of global importance, with both medicinal and economic implications. Selecting the right scientific and systematic approach to biological evaluation of plant products, based on their use in traditional medicine is the key to ideal development of new drugs from plants. One such plant is *Averrhoa carambola* (Oxalidaceae), traditionally known as 'kamrakh' and commonly known as star fruit because of its peculiar shape It has widely been used in Ayurveda, preparations of its fruit and leaves are used to pacify impaired kapha, pitta, skin diseases, pruritis, worm infestations, diarrhea, vomiting, hemorrhoids, intermittent fever, over-perspiration and general debility. It is also used in traditional medicines in countries like India, China, Phillipines, Brazil for various ailments. Although review articles on this plant are already published, but the present attempt is to review and compile all the updated information on botany, phytochemical and pharmacological properties, drug interaction, contraindication and toxicity studies of Averrhoa carambola. These results are very encouraging and indicate that this plant should be studied more extensively to confirm the reproducibility of these results and also to reveal other potential therapeutic effects, along with some "leads" with possible isolation of active biomoieties and their mechanism of action.

10.Sultan et al .,2013. Explained Averrhoa carambola L. (Oxalidaceae), commonly known as star fruit bears a great significance in traditional medicine. Traditionally, A. carambola was used in ailments such as arthralgia, chronic headache, boils and pyodermas, colds, cough, epistaxis, spermatorrhea, fever, food poisoning, gastroenteritis, malaria, malarial splenomegaly, oliguria, postpartum edema, sore throat, subcalorism and traumatic injury. Pharmacological investigations on A. carambola have demonstrated anti-inflammatory, antimicrobial, antifungal, antitumor and anti-ulcer activities. In addition, the

plant possesses hypocholesterolemic, hypoglycemic, hypotensive, nephrotoxic, neurotoxic, negative inotropic and chronotropic effects. Phytochemical investigations have shown the presence of saponins, tannins, alkaloids and flavonoids. This review is an effort to update the pharmacological activities and clinical studies on A. carambola.

11.Shareen et al., 2012. *Averrhoa carambola L. (Oxalidaceae),* Ficus hispida L.f. (Moraceae), and Syzygium samarangense (Blume) Merr. & L.M. Perry (Myrtaceae) are three common plants in Bangladesh, the fruits of which are edible. The leaves and fruits of A. carambola and F. hispida are used by folk medicinal practitioners for treatment of diabetes, while the leaves of S. samarangense are used for treatment of cold, itches, and waist pain. Since scientific studies are absent on the antihyperglycemic effects of the leaves of the three plants, it was the objective of the present study to evaluate the antihyperglycemic potential of methanolic extract of leaves of the plants in oral glucose tolerance tests carried out with glucose-loaded mice. The extracts at different doses were administered one hour prior to glucose administration and blood glucose level was measured after two hours of glucose administration (p.o.) using glucose oxidase method. Significant oral hypoglycemic activity was found with the extracts of leaves of all three plants tested. The fall in serum glucose levels were dose-dependent for every individual plant, being highest at the highest dose tested of 400 mg extract per kg body weight. At this dose, the extracts of A. carambola, F. hispida, and S. samarangense caused, respectively, 34.1, 22.7, and 59.3% reductions in serum glucose levels when compared to control animals. The standard antihyperglycemic drug, glibenclamide, caused a 57.3% reduction in serum glucose levels versus control. Among the three plants evaluated, the methanolic extract of leaves of S. samarangense proved to be the most potent in demonstrating antihyperglycemic effects. The result validates the folk medicinal uses of A. carambola and F. hispida in the treatment of diabetes, and indicates that the leaves of S. samarangense can also possibly be used for amelioration of diabetes-induced hyperglycemia.

12.Daniela et al., 2011. Briefed Inflammatory skin disorders, such as psoriasis and atopic dermatitis, are very common in the population; however, the treatments currently

available are not well tolerated and are often ineffective. *Averrhoa carambola* L. (Oxalidaceae) is an Asian tree that has been used in traditional folk medicine in the treatment of several skin disorders. The present study evaluates the topical anti-inflammatory effects of the crude ethanolic extract of *A. carambola* leaves, its hexane, ethyl acetate, and butanol fractions and two isolated flavonoids on skin inflammation. Anti-inflammatory activity was measured using a croton oil-induced ear edema model of inflammation in mice. Topically applied ethanolic extract reduced edema in a dose-dependent manner, resulting in a maximum inhibition of 73 ± 3% and an ID50 value of 0.05 (range: 0.02–0.13) mg/ear. Myeloperoxidase (MPO) activity was also inhibited by the extract, resulting in a maximum inhibition of 60 ± 6% (0.6 mg/ear). All of the fractions tested caused inhibition of edema formation and of MPO activity. Treatment with the ethyl acetate fraction was the most effective, resulting in inhibition levels of 75 ± 5 and 54 ± 8% for edema formation and MPO activity, respectively. However, treatment of mice with isolated compounds [apigenin-6-*C*-*β*-l-fucopyranoside and apigenin-6-*C*-(2__-*O*-*α*-l-rhamnopyranosyl)-*β*-l-fucopyranoside] did not yield successful results. Apigenin-6-*C*-(2 -*O*-*α*-l-rhamnopyranosyl)-*β*-l-fucopyranoside caused only a mild reduction in edema formation (28 ± 11%). Taken together, these preliminary results support the popular use of *A. carambola* as an anti-inflammatory agent and open up new possibilities for its use in skin disorders.

13.Sandipan Mazumder et al 2013., detailed Different parts of the plant Averrhoa carambola L. is used for the treatment of various disease/disorder (s) by ethnic communities from North Maharashtra and Sonowal Kachari tribes of Dibrugarh, Assam. Still no scientific study is available about the hepatoprotective effect of the leaf of this plant. Present investigation aims to illustrate the hepatoprotective and antioxidant profile of leaves of Averrhoa carambola on carbon tetrachloride induced hepatic damage in mice. To achieve the objective, extracts were subjected to phytochemical screening. The leaf extract was then tested for its oral toxicity which was followed by evaluation of hepatoprotective and antioxidant activity at a dose level of 100mg/kg bw, 200mg/kg bw and 400mg/kg bw orally. Moreover, the hepatoprotective effect was further sustained by validating the leaf extract against different pharmacological parameters. Leaf extract of A.carambola possess

phytoconstituents like alkaloids, tannins, reducing sugar and flavonoids. The extract did not any show any sign of toxicity. The pre-treatment of extract had significantly controlled the levels of serum biochemical and antioxidant enzymes. Finally the grades of hepatoprotectivity were further confirmed while experimenting against other parameters. Finally it can be concluded that the study demonstrates hepatoprotective and antioxidant activity of leaf of Averrhoa carambola and thus supports its usage in traditional medicine.

14.Tanzirr et al., 2017 . Phytochemical analysis of the ethanolic leaf extract of Averrhoa carambola Linn. Indicated the presence of carbohydrate, glycosides, steroid, saponins, flavonoids, gum, tannins and the absence of reducing sugars. On acetic acid induced analgesic test, the plant extract exhibited a significant writhing reflex inhibition by 11.12% and 40.28% (p 0.01) at the dose of 250 mg/kg and 500 mg/kg body-weight respectively while the standard drug diclofenac sodium inhibition was found to be 69.45% at a dose of 25 mg/kg body weight. The plant extract showed moderate level of antimicrobial activity against Streptococcus agalactiae, Streptococcus pyogenes, Shigella dysenteriae, Pseudomonas spp., Staphylococcus saprophyticus when Kanamycine was applied at the dose of 30 µg/disc. On qualitative in vitro antioxidant assay (2, 2-diphenyl-1-picryl hydrazyl (DPPH) method), the ethanolic leaf extract was found to have potent antioxidant compounds. In the castor oil-induced diarrhoeal mice, the plant extract significantly reduced the number of stools by 25% and 31.25%.

15.Ritu singh et al., 2014. Liver cancer remains one of the severe lethal malignancies worldwide and hepatocellular carcinoma (HCC) is the most common form. The current study was designed to evaluate the prophylactic role of the fruit of Averrhoa carambola (star fruit or Kamrak) on diethylnitrosamine- (DENA-) induced (15 mg/kg b.wt.; single i.p. injection) and CCl_4-promoted (1.6 g/kg b.wt. in corn oil thrice a week for 24 weeks) liver cancer in Swiss albino mice. Administration of ACE was made orally at a dose of 25 mg/kg b.wt/day for 5 consecutive days and it was withdrawn 48 hrs before the first administration of DENA (preinitiational stage). CCl_4 was given after 2 weeks of DENA administration. A cent percent tumor incidence was noted in carcinogen treated animals while ACE administration resulted in a

considerable reduction in tumor incidence, tumor yield, and tumor burden. Further, ACE treatment brings out a significant reduction in lipid peroxidation () along with an elevation in the activities of enzymatic antioxidants (superoxide dismutase, , and catalase,), nonenzymatic antioxidant (reduced glutathione,), and total proteins () when compared to the carcinogen treated control. These results demonstrate that ACE prevents the DENA/CCl_4 induced adverse physical and biochemical alterations during hepatic carcinogenesis in mice. This study suggests the prophylactic role of Averrhoa carambola against hepatocellular carcinoma in mice; therefore, it could be employed for the further screening as a good chemopreventive natural supplement against cancer.

PLANT PROFILE

Averrhoa carambola

Star Fruit

Classification of Averrhoa carambola

Scientific Name: Averrhoa carambola

Kingdom Plantae – Plants

Subkingdom Tracheobionta – Vascular plants

Superdivision Spermatophyta – Seed plants

Division Magnoliophyta – Flowering plants

Class Magnoliopsida – Dicotyledons

Subclass Rosidae Order Geraniales

Family Oxalidaceae – Wood-Sorrel

family Genus Averrhoa Adans. – averrhoa Species Averrhoa carambola L. – carambola

Nomenclature, The carambola is known under different names in different countries. It should not be confused with the closely related bilimbi, with which it shares some common names[9,10,11].

Bengali – kamranga

Assamese - kordoi

Marathi – karambal

Telugu - ambanamkaya

English - carambola, starfruit

Filipino - balimbing, saranate

Hindi – kamrakh

Gujarati – kamrakh

Malayalam – chathurapuli

Tamil - thambaratham

Indonesian – belimbing

Malay – belimbing

Sylheti – khafrenga

Sinhala – Kamaranga

Vietnamese - khế

Figure 5. Leaves of *Averrhoa carambola[*

Figure 6. Fruits of *Averrhoa carambola*

Figure 7. Fruits and stems of *Averrhoa carambola*

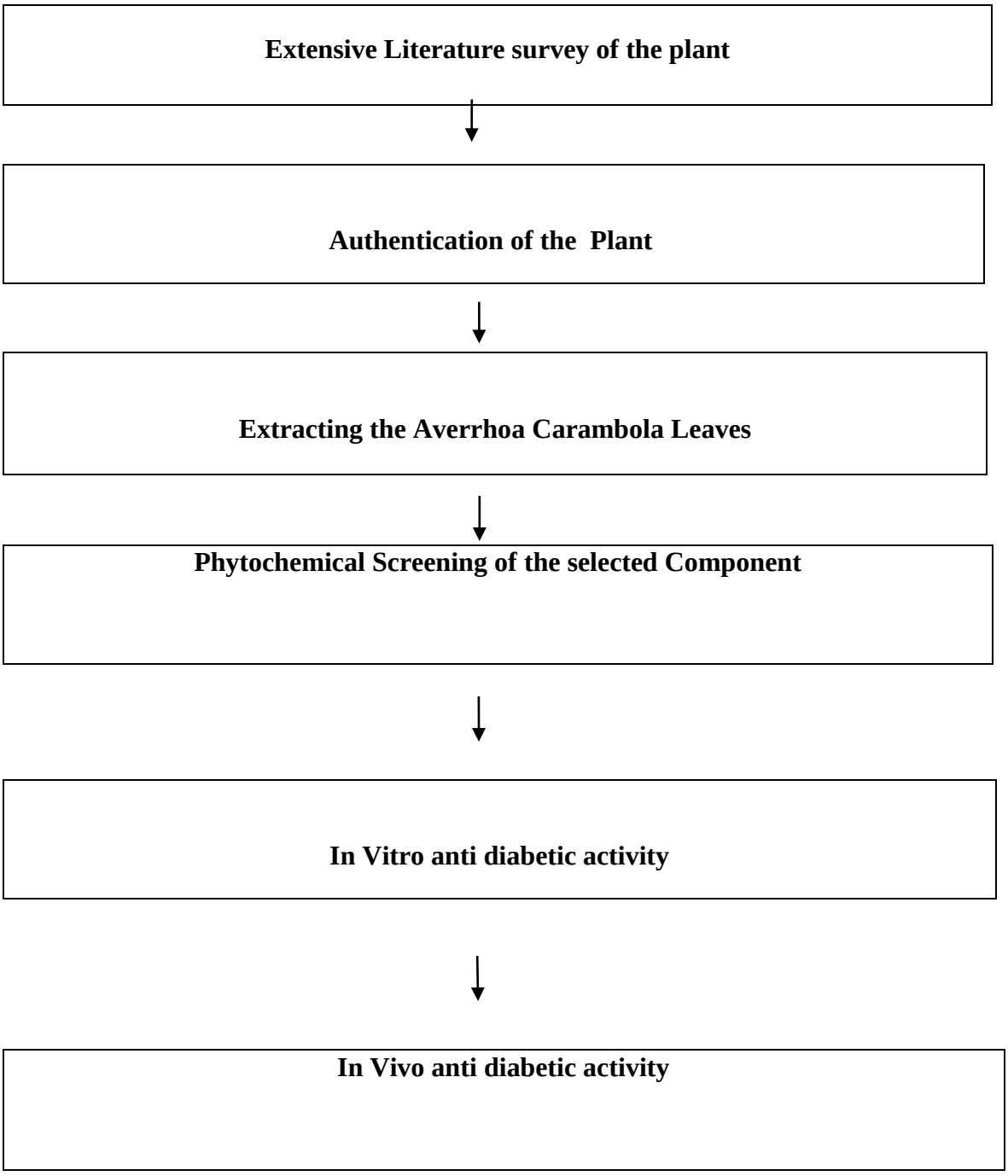
3.AIM AND OBJECTIVE

Reason for choosing diabetes mellitus that few medications in clinical practice for the treatment, a hefty portion of these oral hostile to diabetic segment have been accounted for to demonstrate genuine antagonistic side effects. It is obvious that because of the reactions of the presently utilized medications, there is a requirement for a strong medication with negligible unfavorable impacts, which can be taken for long time. Plant materials which are being utilized as customary pharmaceutical for the treatment of diabetes are viewed as one of the great barriers for another medication or a prompt make another medication. All through the world numerous conventional plant medicines for diabetes exists. In any case, few have gotten logical or therapeutic investigation and the WHO has prescribed that customary plant medications for diabetes warrant promote assessment and logical approval. Presently I have under taken the investigation of "Assessment of antidiabetic of alcoholic, petroleum ether and ethyl acetate concentrates of Averrhoa carambola leaves on Streptozotocin induced diabetic rats. To meet this aim we framed following objectives.

OBJECTIVES

1. To Extract the Averrhoa carambola using different solvent by Mantox Hapter
2. To Study the prelimmery phyto chemical screening of Averrhoe carambola
3. To Evaluate the In vitro Anti diabetic study of Averrhoe carambola
4. To Evaluate the In vivo Anti diabetic study of Averrhoe carambol

4.PLAN OF THE WORK



5. MATERIALS AND METHODS

A) Plant collection and authentification

The leaves of *Averrhoa carambola* were collected from Anantgiri forest, Hyderabad

B) Preparation of coarse powder and Extraction technique

The leaves were shade dried at room temperature for 10 days. Then these were milled into powder by mechanical grinder. This powder was sequentially extracted to their increasing polarity with Petroleum ether, Ethyl acetate, Ethanol respectively. About 500gm of powdered leaf was uniformly packed into a thimble in a soxhlet apparatus and extracted with 1000ml Petroleum ether, Ethyl acetate and Ethanol, respectively. Constant heat was provided by Mantox heater for recycling of the solvent. The process of extraction continues for 1-2 hours for each solvent. The excess solvent was evaporated and the dried extracts were kept in refrigerator at 4ºC for their future use in phytochemical analysis and pharmacological screenings.

D) Preliminary phytochemical screening of ethanolic leaf extracts of *Averrhoa carambola*

The ethanolic leaf extract of *Averrhoa carambola* was used for testing preliminary phytochemical screening in order to detect major chemical groups.

Test for carbohydrates

- Molisch's test: Dissolved small quantity of 300mg alcoholic and dried leaf extract powder of Pimenta dioica separately in 4ml distilled water and filtered. The filtrate was subjected to Molisch's test.
- Fehling's test: Dissolve a small portion of extract in water and treat with Fehling's solution.

- Phenols test: The extract was spotted on a filter paper. A drop of phosphomolybdic acid reagent was added to the spot and was exposed to ammonia vapours.

Test for flavanoids

- Shinoda test: To 2 to 3ml of extract, a piece of magnesium ribbon and 1ml of concentrated HCl was added.
- .Lead acetate test: To 5ml of extract 1ml of lead acetate solution was added.

Test for tannins

- Braemer's test: To a 2 to 3ml of extract, 10% alcoholic ferric chloride solution was added.

Test for steroid/terpenoid

- Liebermann-Burchardt test: To 1ml of extract, 1ml of chloroform, 2 to3ml of acetic anhydride and 1 to 2 drops of concentrated Sulphuric acid are added.

Test for alkaloids

.Draggendorf's test: A drop of extract was spotted on a small piece of precoated TLC plate and the plate was sprayed with modified Draggendorf's reagent.

- Hager's test: The extract was treated with few ml of Hager's reagen.
- Wagner's test: The extract was treated with few ml of Wagner's reagent.

Tests for Glycosides

- Legal's test: Dissolved the extract [0.1g] in pyridine [2ml], added sodium nitroprusside solution [2ml] and made alkaline with Sodium hydroxide solution.

Test for Saponins

- Foam test: 1ml of extract was dilute with 20ml of distilled water and shaken with a graduated cylinder for 15 minutes.

Test for Anthraquinones

- Borntrager's test: About 50 mg of powdered extract was heated with 10% ferric chloride solution and 1ml of concentrated HCl. The extract was cooled, filtered and the

filtrate was shaken with diethyl ether. The ether extract was further extracted with strong ammonia.

Test for Amino acids

- Ninhydrin test: Dissolved a small quantity of the extract in few ml of water and added 1ml of ninhydrin reagent.

Test for fixed oils and fats

- Press small quantity of the petroleum ether extract between two filter paper.

Note: the results for the above experiments can be noted as follows.

- If the response to the test is high it can be noted as +++which indicates that the particular group is present as the major class.
- If the response is average then note it as ++ indicates the presence in moderate quantity.
- If the response is very small then note it as + indicating the presence of only in traces.
- If no response is then negative.

E) Acute toxicity study

In a research study when a drug is administered to a biological system there will be some interactions may happen .In most case these are desired and usefull,but many effects are not advantageous. Acute, subacute and chronic toxicity studies are performed by the manufacturers in the investigation of a new drug.Acute toxicity is involved in estimation of LD_{50}(It is the lethal dose (cuasing death)to 50% of tested group animals)[54].

LD_{50} (median lethal oral dose)

LD_{50} (median lethal oral dose) is a statistically derived oral dose of a substance that can be expected to cause death in percent of animals when administered by the oral

route.The LD_{50} value is expressed in terms of weight of test substance per unit weight of animal(mg/kg)

In this study acute toxicity study was carried out in wistar albino rats.The procedure was followed by using OECD 423(Acute toxic class method).The rats are fasted overnight, prior to dosing. The three dose levels are administered by the help of oral feeding needle over the prior of 24 hours.After the drugs has been administered,food may be with held for a further 3-4 hours in rats.The purpose of sighting study is to allow selection of the appropriate starting dose for main study.The test substabce is administered to a single animal in a sequential manner following from the fixed dose levels of 5,50,300 and 2000mg/kg. The interval between dosing of each level is determined by the mortality/onset,duration and severisty of toxic signs over the period of 24 hours,special attention given during the first 4 hours.Four hours after the drug administration,provide the food and water for 14 days and daily observed some parameters such as food intake,water intake,mortality,onset,Duration and severity of toxic signs.The animal weight is recorded on weekly once.On the day fourteen all the animals are sacrificed,to isolate the organs and observe the histopathological changes.Based on the mortality result of sighting is decided and carried out with five animals per dose level (5 or 50 or 300 or 2000mg/kg).Based on the mortality result on 14^{th} day of observation,the doses for invivo study are selected.

F*) Invitro* antidiabetic activity of *Averrhoa carambola* leaf extracts

Alpha-amylase inhibition assay

Chemicals or reagents

Potato starch, trichloroacetic acid, Folin-Ciocalteau reagents were purchased from SD Fine Pvt. Ltd., Mumbai, 3,5-dinitrosalicylic acid, Tris buffer, linoleic acid, ammonium molybdate, were purchased from Hi-Media Pvt. Ltd., Mumbai, α-amylase, α-glucosidase enzymes, xanthine oxidase, quercetin, hypoxanthine, pyrocatechol were purchased from SRL Pvt. Ltd., Mumbai. Glucose assay kit from Agappe diagnostic Pvt. Ltd., Kerala, Acarbose was obtained from Bicon Pvt. Ltd., Chennai, ferrozine, (2'2-azobis (2-amidino

propane) dihydrochloride), butylated hydroxy toluene from Loba Cheme. All other chemicals used in the study were obtained commercially and were of analytical grade.

Instrument used

UV-visible Spectrometer (Systronic double beam- UV-2201).

Preparation of extract

Leaf extractions used in invitro and invivo studies were prepared by using suitable solvents (Carboxy methyl cellulose).

Experimental procedure for α-amylase inhibition assay

A total of 500 µl of test samples and standard drug (100-1000µg/ml) were added to 500 µl of 0.20 mM phosphate buffer (pH 6.9) containing α-amylase (0.5mg/ml) solution and were incubated at 25°C for 10 min. After these, 500 µl of a 1% starch solution in 0.02 M sodium phosphate buffer (pH 6.9) was added to each tube. The reaction mixtures were then incubated at 25°C for 10 min. The reaction was stopped with 1.0 ml of 3, 5 di nitro salicylic acid colour reagent. The test tubes were then incubated in a boiling water bath for 5 min, cooled to room temperature. The reaction mixture was then diluted after adding 10 ml distilled water and absorbance was measured at 540 nm. Control represent 100% enzyme activity and were
conducted in similar way by replacing extract with vehicle.

Calculation of 50% inhibitory concentration (IC_{50})

The concentration of the plant extracts required to scavenge 50% of the radicals (IC_{50}) was calculated by using the percentage scavenging activities at five different concentrations of the extract. Percentage inhibition (I %) was calculated by

$$I\ \% = \frac{(Ac-As)}{Ac} \times 100$$

where,

Ac = Absorbance of the control,

As = Absorbance of the sample.

G) *Invivo* (antidiabetic activity) of Averrhoa *carambola* leaf extract in STZ induced diabetic wistar albino rats.

Wistar albino rats (150- 200 grams) of both sexes were procured from Sura (labs, Ameerpet, hyderabad, India.) Prior to the experiment the rats were housed in a clean polypropylene cages (6 rats/ cages) for a period of 7 days under standard temperature (25 - 30^{o} c) , relative humidity (45 – 55%), dark / light cycle (12 /12 hrs). The studies were performed with the approval of Organisational Animal Ethics Committee (OAEC) (ULSB/DAEC/KER/678/333/17). The animals were put in overnight fasting were deprived of food for 16 hrs but allowed free access of water.

Treatment Protocol

S.no	**Group**	**Treatment**
1.	Control (cmc)	Received only CMC
2.	Positive control(cmc)	STZ
3.	Extrat 200 of Averrhoa carambola	Ethanolic extract of Extrat 200 of Averrhoa carambola
4.	Extract 400 Averrhoa carambola	Ethanolic extract of Extrat 400 of Averrhoa carambola

Statistical Analysis

All values are expressed as mean ± SEM. Statistical analysis was performed by One-way Anova followed by Dunnet's t-test using SPSS version 17. A 'p' value less than 0.05 was considered significant.

Research Outcomes

Study of antidiabetic activity of an albino rat model as significant improvement was observed

6. RESULTS AND DISCUSSION

A) Appearance and percentage yield of EEHC(Ethanolic Extract of Averrhoa carambola leaves)

Ethanolic extract of *Averrhoa carambola* was a semisolid brownish colour extract and the percentage yield was found to be 14.35%.

B) Phytochemical studies

S.No	Compounds	Testing	Inferences
	Carbohydrates	Molisch's test Fehling's test	 -
	Phenols	Phosphomolybdic acid test	+++
	Flavonoids	Shinoda test Lead acetate test	 ++ ++
	Tannins	Braemer's test	_
	Alkaloids	Wagner's Mayer's Draggendrof's test	+ + +
	Glycosides	Legal's test Brontranger's test	+ + +
	Saponins	Foam test	+
	Sterols	Salkowski's test	_
	Amino acids	Ninhydrin test	_
	Terpenoids	Lieberman Burchardt test	+

Table 8. Results of ethanolic extract of *Averrhoa carambola*

+ In traces

++ Present in moderate amount

+++ More amounts is present

-Absence

The phytochemical studies results revealed that the Molisch's test no characteristic observation indicated the absence of carbohydrates, by phosphomolybdic acid test Blue coloration of the spot indicated the presence of phenols. Shinoda test and Lead acetate test gave pink or red coloration of the solution indicated the presence of flavonoids Flocculent white precipitate also indicated the same. There is no dark blue or greenish grey coloration of the solution indicated the absence of of tannins in the drug. No characteristic observation for steroids and dark pink or red coloration of the solution indicated the presence of terpenoids. Orange coloration of the spot indicated the presence of alkaloids. Yellow or reddish brown precipitation precipitation indicated the presence of alkaloids. Pink to red colour solution indicates the presence of glycosides. No layer of foam formation indicates the absence of Saponins. If the response to the test is indicated table-1high it can be noted as++++ or +++ which indicates that the particular group is present as the major class. If the response is average then note it as ++ indicates the presence in moderate quantity and note it as + indicating the presence of only in traces. If no response is then negative.

C) Acute Toxicity

Acute toxicity study result shows that there is no morbidity and modality at 2000mg/kg animal body weight. Hence it can be used for clinical utility.

D) *invitro* antidiabetic study

Conc (mcg/ml)	Percentage Inhibition
0	0
25	34
50	39
75	46
100	58
125	62

Table 4. α-Amylase Inhibition of Petroleum Ether extract of *Averrhoa carambola* leaves

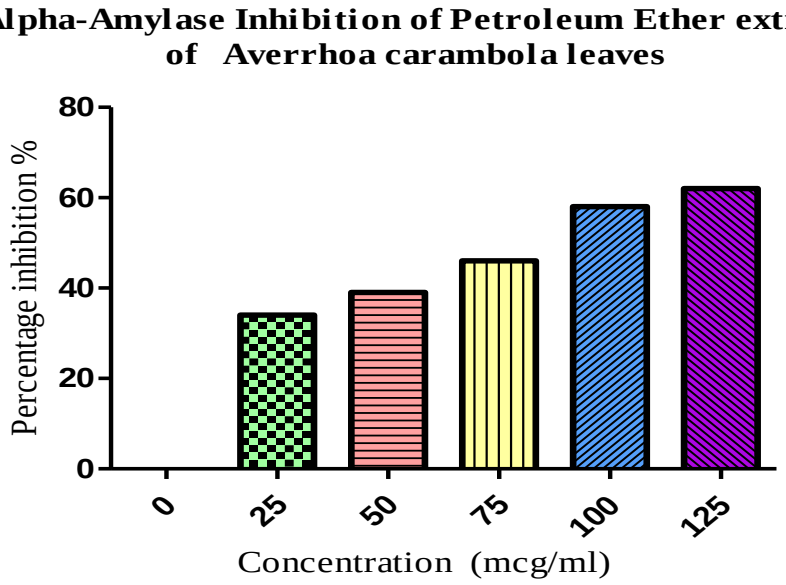


Fig 8. Alpha-amylase Inhibition of Petroleum ether extract of *Averrhoa carambola* leaves

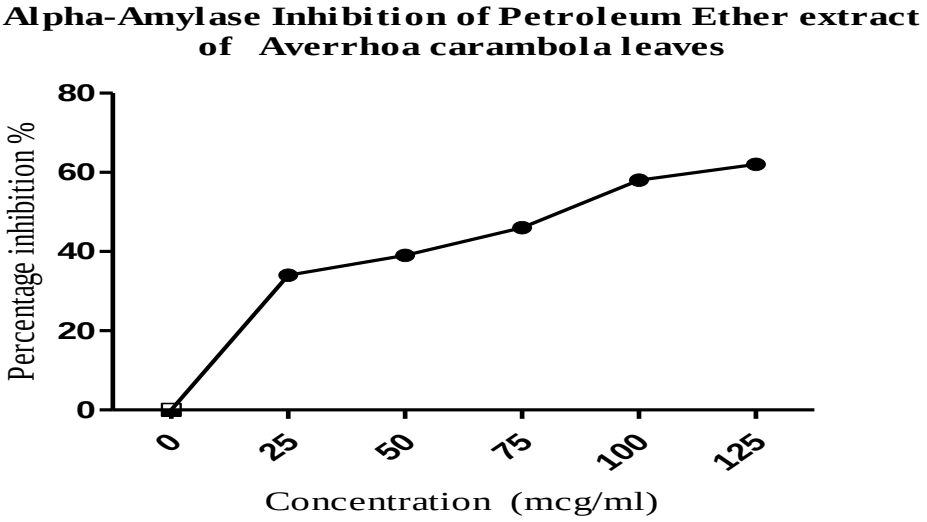


Fig 9. Graphical representation of Alpha-amylase Inhibition of Petroleum ether extract of *Averrhoa carambola* leaves

Conc (mcg/ml)	Percentage Inhibition
0	0
25	40
50	47
75	53
100	61
125	66

Table 5. α-Amylase Inhibition of Ethyl acetate Extract of *Averrhoa carambola* leaves

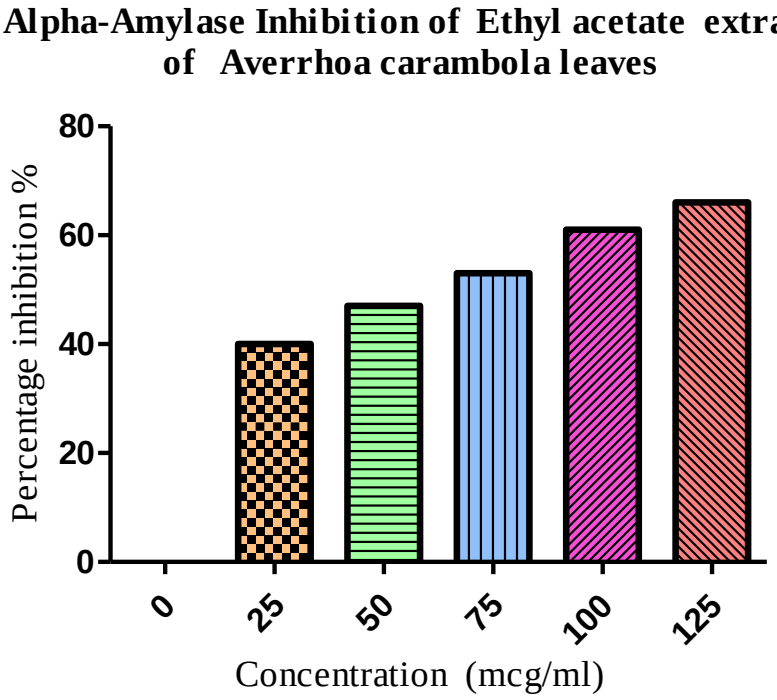


Fig 10. Alpha-amylase Inhibition of Ethyl acetate extract of *Averrhoa carambola* leaves

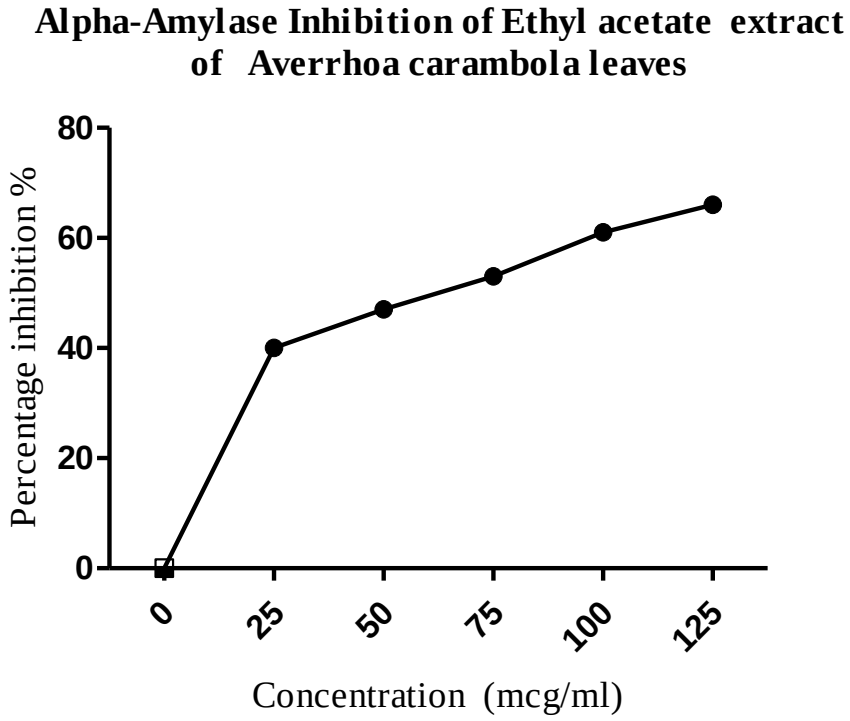


Fig 11. Graphical representation of Alpha-amylase Inhibition of Ethyl acetate extract of *Averrhoa carambola* leaves

Conc (mcg/ml)	Percentage Inhibition
0	0
25	34
50	40
75	53
100	60
125	68

Table 6. α-Amylase Inhibition of Ethanolic Extract of *Averrhoa carambola* leaves

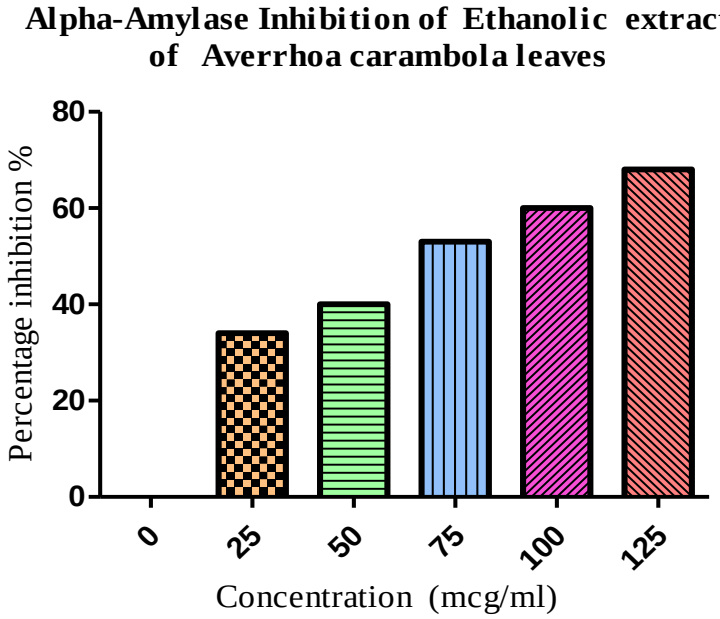


Fig 12. Alpha-amylase Inhibition of Ethanolic extract of *Averrhoa carambola* leaves

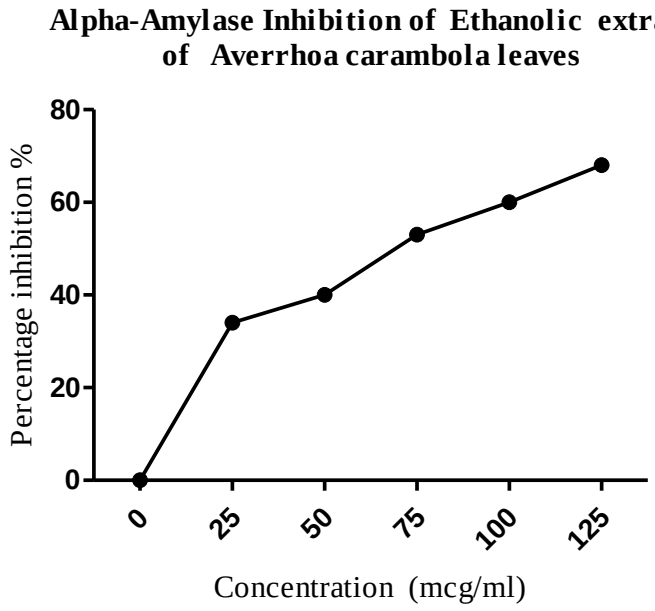


Fig 13. Graphical representation of Alpha-amylase Inhibition of Ethanolic extract of *Averrhoa carambola* leaves

Conc (mcg/ml)	Percentage Inhibition
0	0
25	30
50	49
75	60
100	63
125	73

Table 7. α-Amylase Inhibition of Acarbose (Positive control)

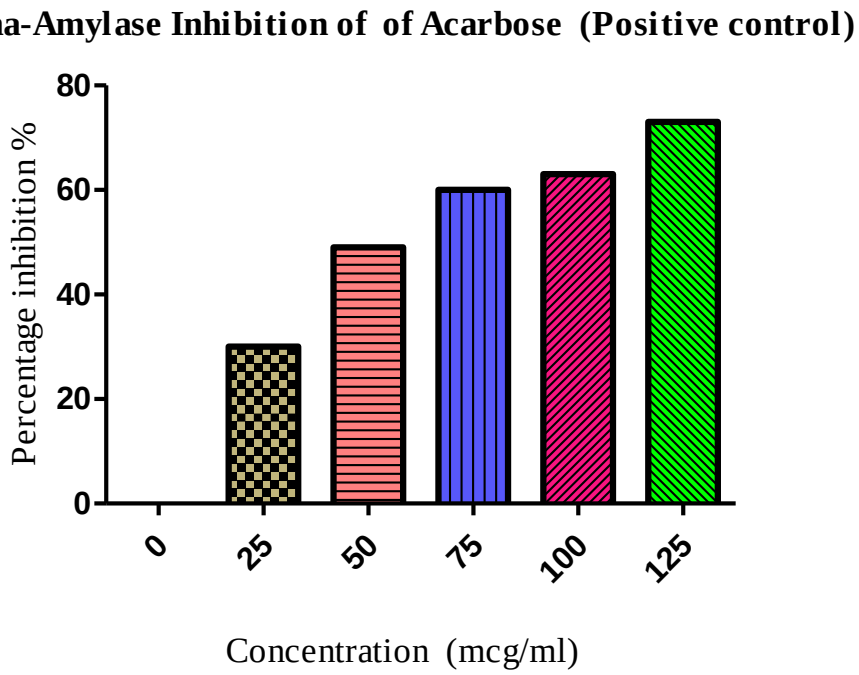


Fig 14. Alpha-amylase Inhibition of positive control

Alpha-Amylase Inhibition of of Acarbose (Positive control)

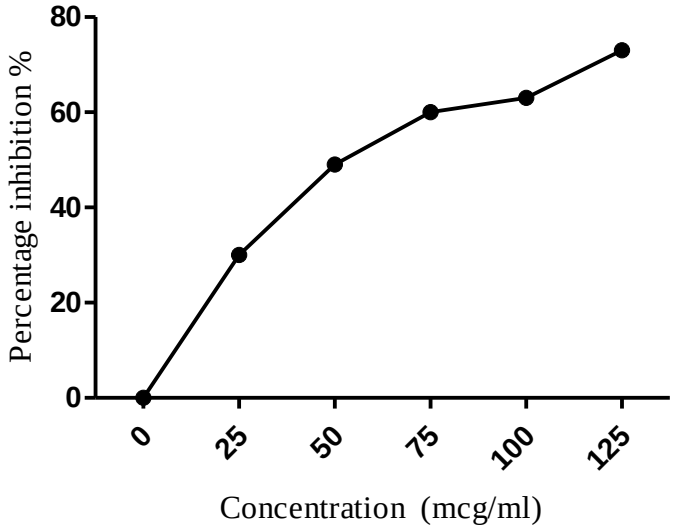


Fig 15. Graphical representation of alpha-amylase Inhibition of positive control

PERCENTAGE OF INHIBITION

Extract	% of Inhibition
Petroleum ether Extract	62%
Ethyl acetate extract	66%
Ethanolic extract	68%
Acarbose	73%

Table 8. Percentage Of Inhibition

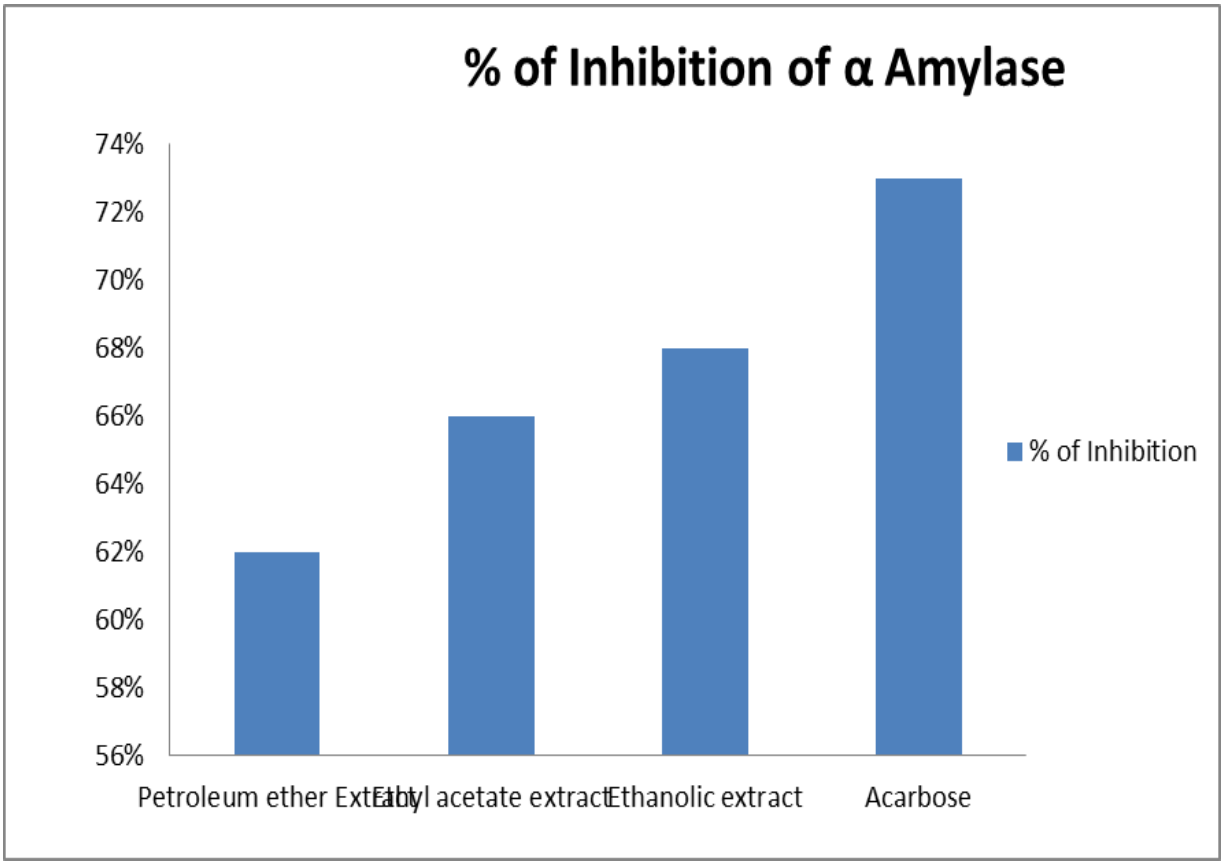


Fig 16. % of inhabitation of Alpha-amylase

Invitro Antidiabetic studies result revels that 125 mcg of all extract shown the significant alpha-amylase Inhibition when compare with other concentration. *In vitro* α amylase studies result revels that increased concentration of all the extract has been shown significant inhibition of α amylase activity hence its dose depend manner. Among all the Extract Ethanolic Extract shown the 68% of Inhibition of α Amylase which similar that of acarbose (standard) 73% of Inhibition of α Amylase.

Anti Diabetic Study

Treatment	Dose mg/kg	Blood Glucose Level (mg/dl)		
		0 min	0.5hr	1 hr
Control (CMC)	0.5 %	67.26±2.51	67.88±1.96	70.56±0.43
Positive Control Glibenclamide	2	67.20±0.04	51.43±1.94	30.29±0.33
Ethanolic Extract of *Averrhoa Carambola*	200	67.00±0.32	52.10±2.56	33.90±0.15
Ethanolic Extract of *Averrhoa Carambola*	400	67.80±0.24	59.32±1.26	58.76±1.43

Table 9. Hypoglycemic Test

The glucose levels were analysed by using glucometer and each value is the mean ± standard error (n= each group consist of 6 animals)($p<0.05$)*, ($p<0.001$)**& ($p<0.0001$)*** as compared to control & positive control group evaluated by one way, ANOVA followed by Dunnet 't' test. (CMC= Carboxy methyl Cellulose)

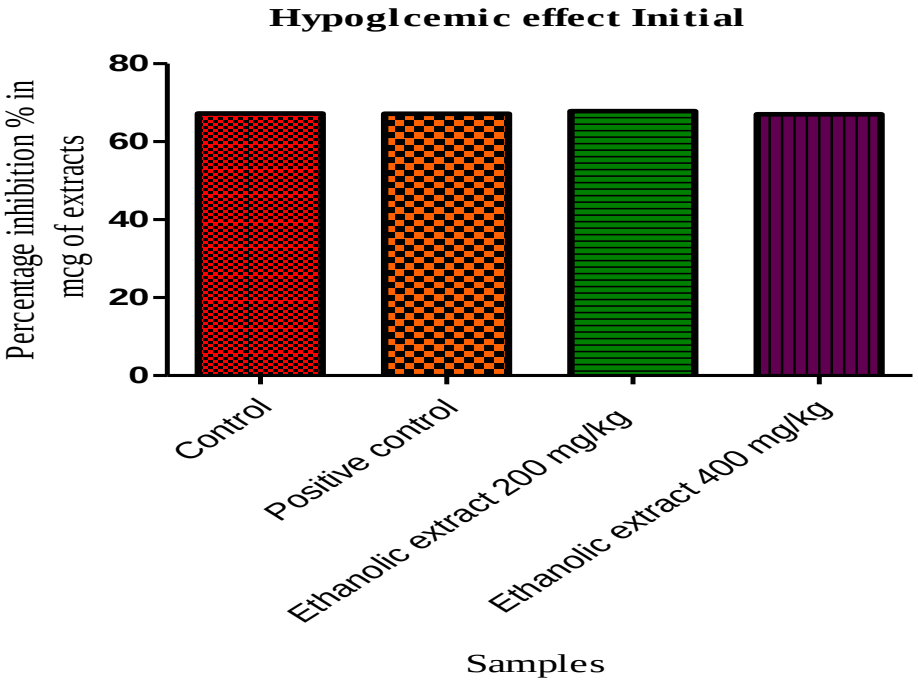


Fig 17. Hypoglycemic effect initia

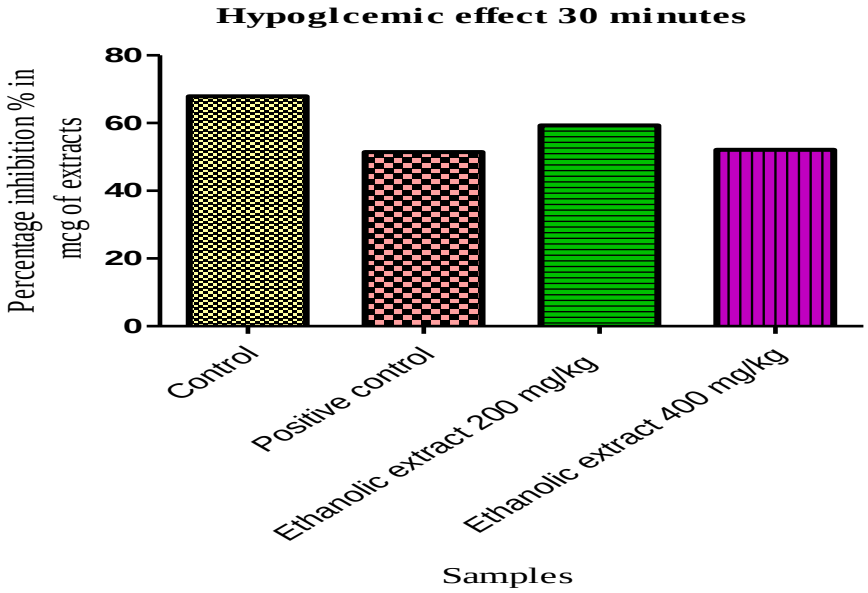


Fig 18. Hypoglycemic effect 30 minutes

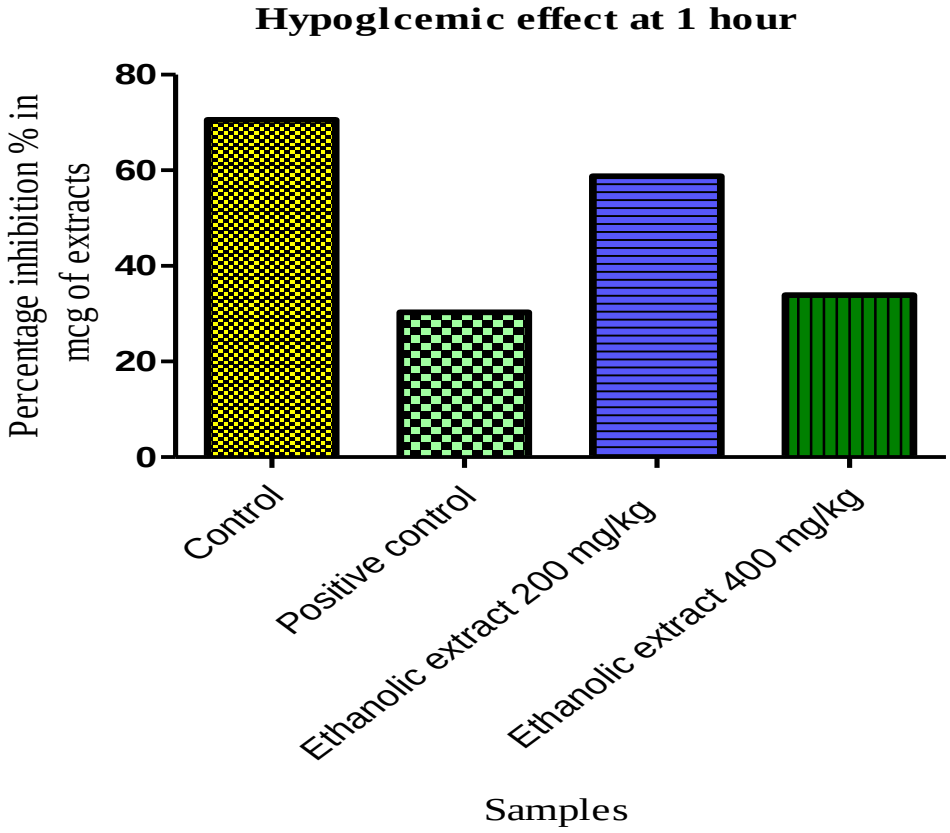


Fig 19. Hypoglycemic effect 1 hour

The hypoglycemic test results have shown Table No:09 which indicated ethanolic extract of *Averrhoa carambola* treated animals 200 & 400, significantly decreased in blood glucose level (33.90±0.15 & 58.76± 1.43) ($P<0.05$)*, ($P<0.001$)**& ($P<0.0001$)*** when compared to control and positive control.

Invivo antidiabetic study

Sl. No.	Treatment	Blood glucose level (mg/dl) day		
		Day 1	Day 7	Day 14
1	Normal control 10 ml/kg P.O	80.56±1.43	76.32±1.65	77.62± 0.26
2	Negative control 100 mg/kg I.P	268.60±0.97	276.34±0.85	279.02±0.23
3	Positive control (Glibenclamide 2mg/kg)	259.32±0.43	182.41±0.29	120.30±0.41
4	Ethanolic Extract of Averrhoa carambola leaves 200 mg/kg	263.04±1.51	257.56±0.42	250.1±1.38
5	Ethanolic Extract of Averrhoa carambola leaves 400 mg/kg	272.09±0.36	180.55±1.45	169.21±0.04

Table 10. Results of the effects of ethanolic extract on blood Glucose levels

(The values were expressed as Mean ± S.E.M. (n=6 animals in each group).

The experimental results have indicated on table No:10. The negative control group glucose levels were significantly increased when compared to each other groups. All the groups of animals were affected in diabetes, which indicated blood glucose levels were slight changes in the blood glucose level for normal control group at 7^{th} and 14^{th} days . On day 7^{th} glucose levels were significantly decreased glibenclamide 2mg/kg treated group when compared with control group at 7^{th} and 14^{th} days. The ethanolic leaves extract of *Averrhoa carambola* treated groups 200 & 400 mg/kg were dose dependent manner decreased when compared with control group but positive control have more anti diabetic activity at 7^{th} day. **The ethanolic leaves extract of *Averrhoa carambola* at the dose level 400mg/kg have equipotent activity when compared with positive control at 7^{th} day**. The ethanolic leaves extract of *Averrhoa carambola* 200 & 400 mg/kg have been expressed dose dependent anti diabetic action when compared to control and positive control. On day 14^{th}, ethanolic leaves extract of *Averrhoa carambola* treated animals 200 & 400 mg/kg significantly decreased and maintain the blood glucose level when compared to control and positive control.

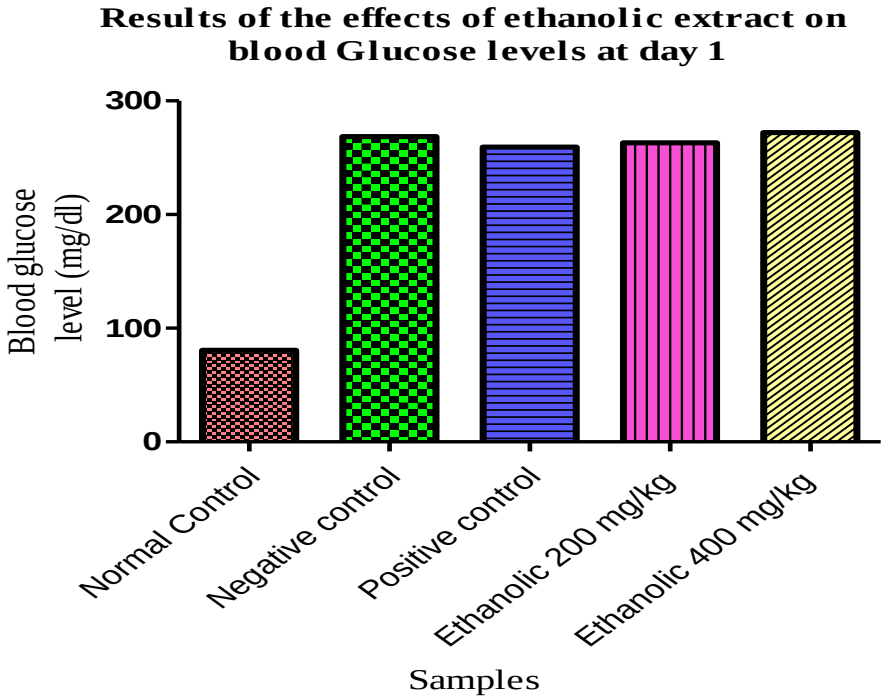


Fig 20. Results of the effects of ethanolic extract on blood Glucose levels at day 1

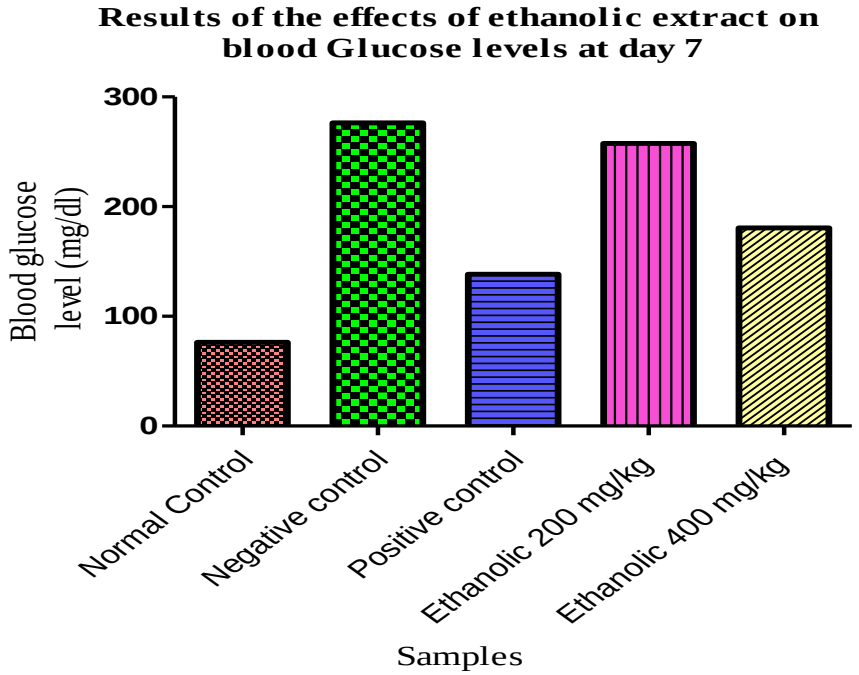


Fig 21. Results of the effects of ethanolic extract on blood Glucose levels at day 7

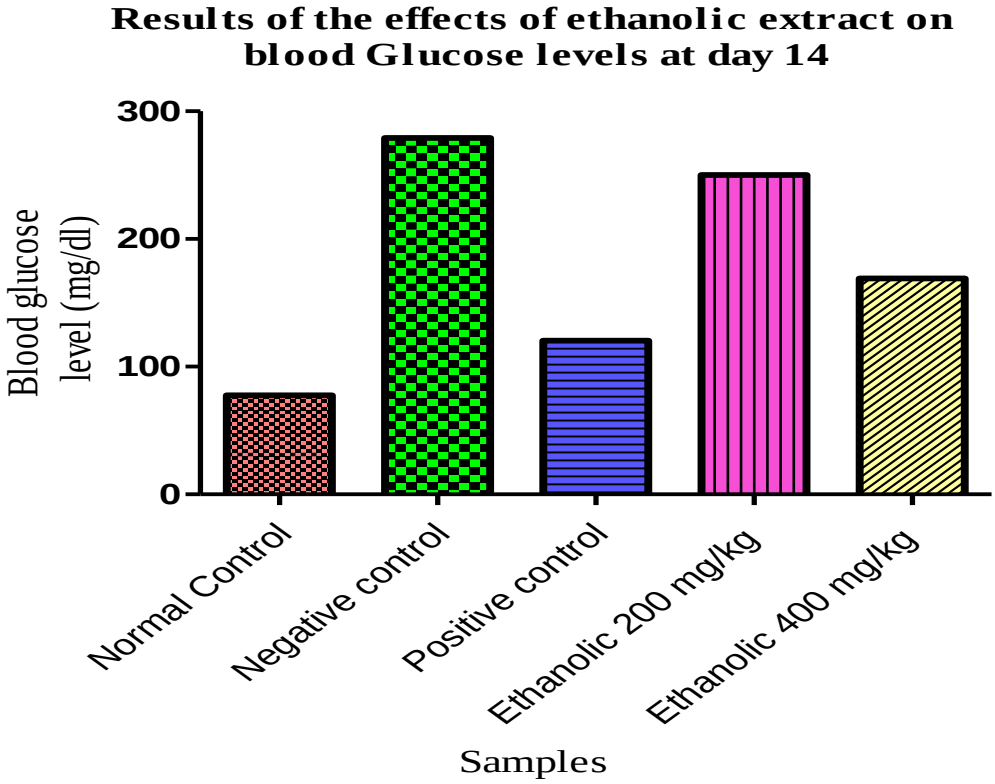


Fig 22. Results of the effects of ethanolic extract on blood Glucose levels at day 14

Treatment	Dose mg/kg	Blood Glucose Level (mg/dl)						
		0 min	0.5hr	1 hr	1.5hr	2 hr	2.5hr	3hr
Control (CMC)	0.5 %	69.29±0.39	146.73±0.05	191.49±0.64	176.62±0.23	161.03±2.68	158.03±2.25	133.41±3.30
Positive Control Glibenclamide	2	69.12±0.32	109.42±3.55	116.60±5.50	99.59±1.04	87.42±1.29	81.02±0.58	79.01±0.32
Ethanolic Extract of *Averrhoa carambola*	200	70.45±2.32	134.02±1.04	153.72±0.26	143.03±0.03	132.50±0.03	117.05±0.06	116.03±2.37
Ethanolic Extract of *Averrhoa carambola*	400	70.23±2.429	120.42±1.62	127.3±0.36	108.38±0.43	97.09±0.54	91.53±0.03	89.04±0.43

Table 11 - Oral Glucose Tolerance Test

The glucose levels were analyzed by using glucometer and all values are expressed as Mean±SEM (n=6), Group 2 was compared with group 1, Groups —3,4 were compared with group 2; *p<0.05, **p<0.01,p<0.001*** evaluated by one way, ANOVA followed by Dunnet 't' test.

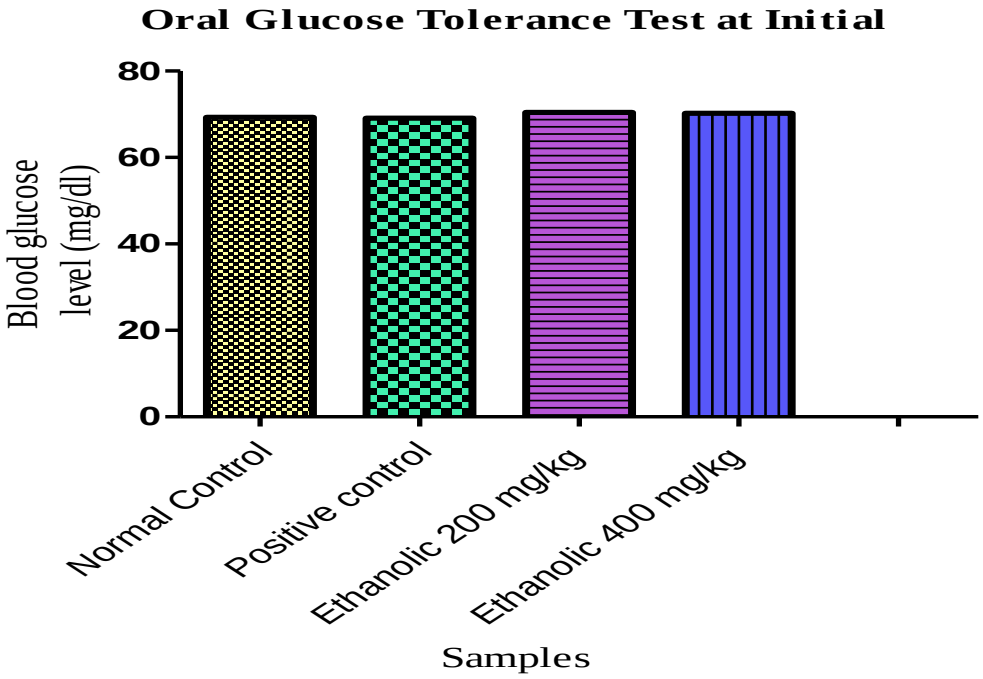


Fig.23 OGTT initial

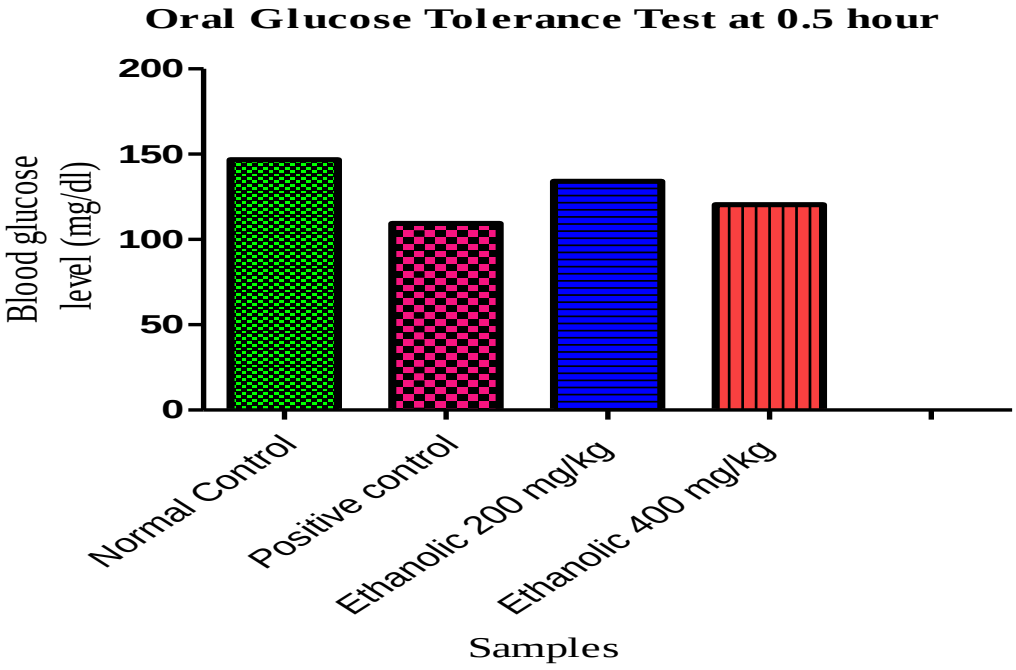


Fig 24. OGTT 30 minutes

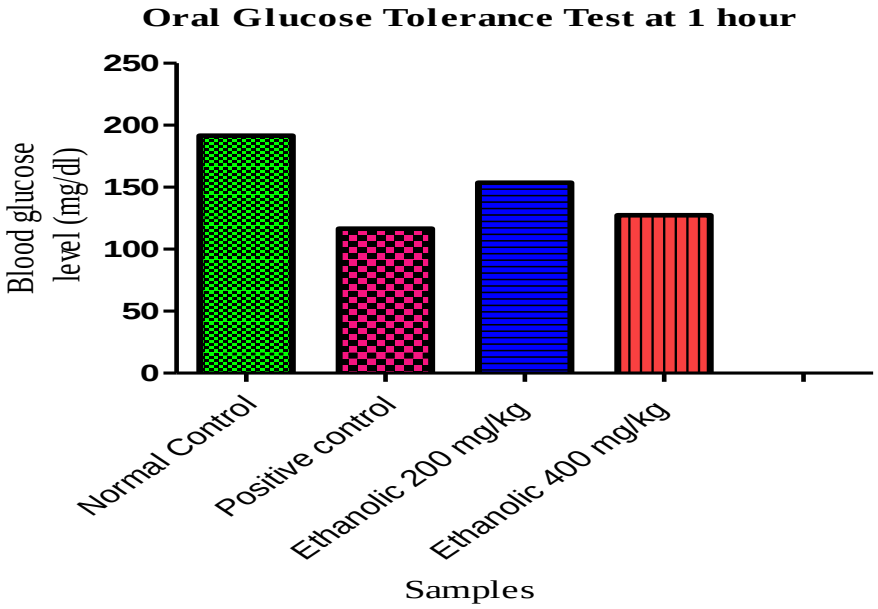


Fig 25. OGTT one hourly

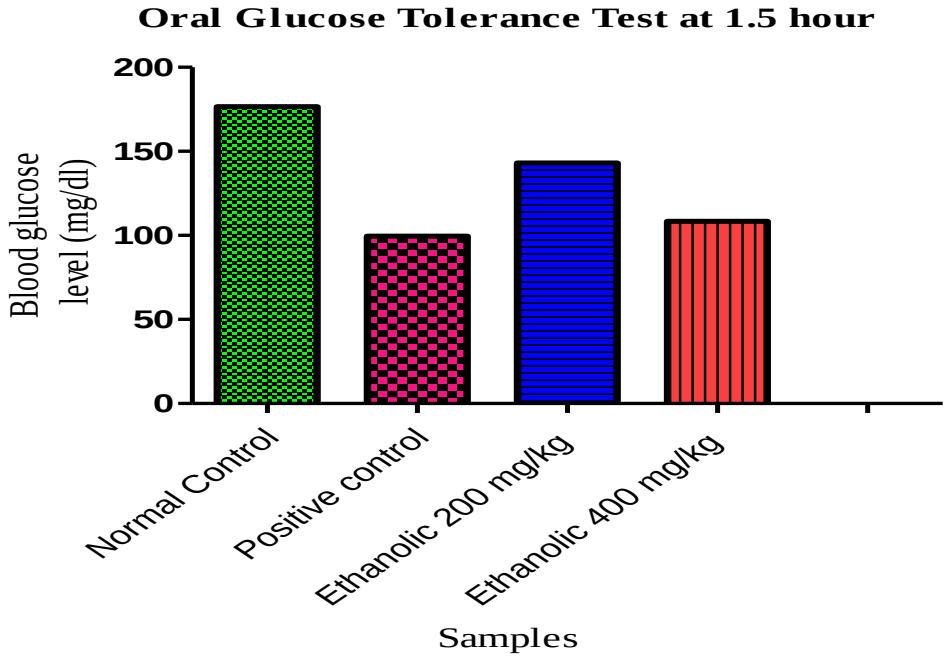


Fig 26. OGTT 1.5 hourly

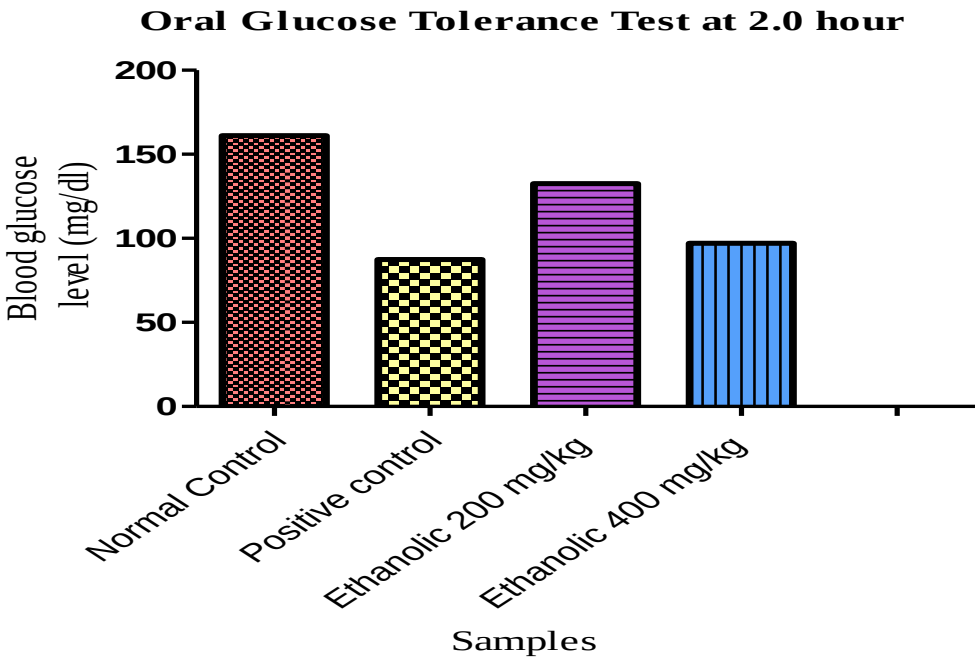


Fig 27. OGTT 2.0 hourly

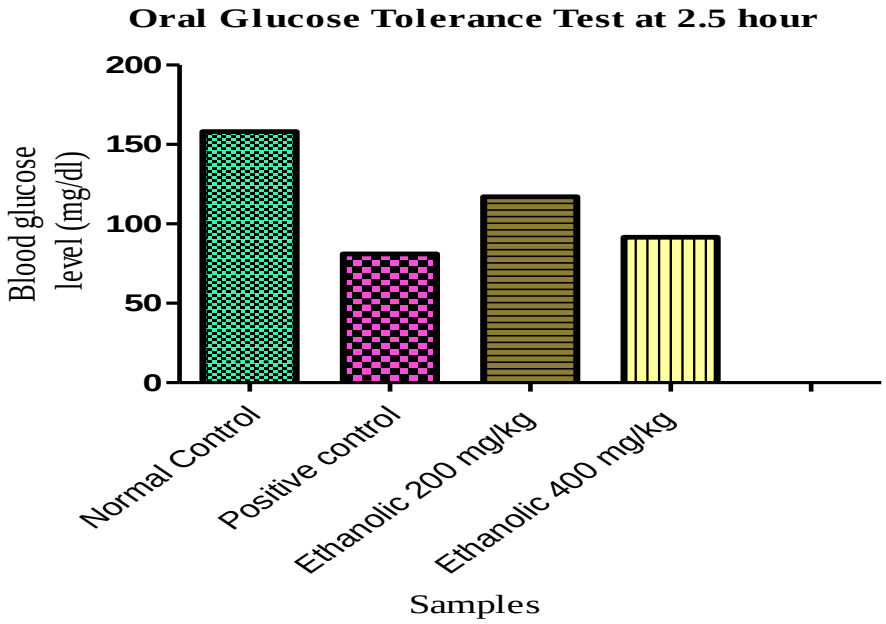


Fig 28. OGTT 2.5 hourly

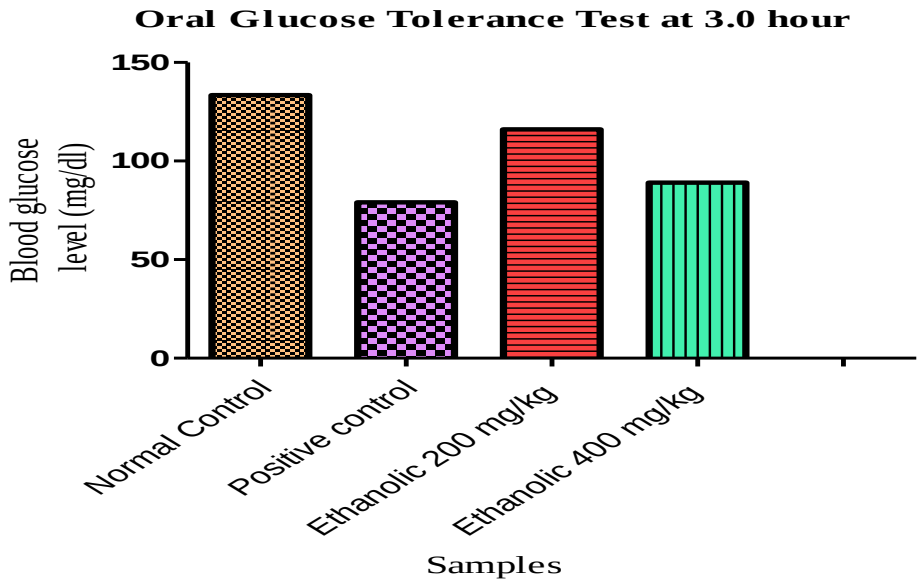


Fig 29. OGTT 3.0 hourly

Oral Glucose Tolerance Test (OGTT) results have been expressed, half hour after the glucose treatment, all the groups of animal blood glucose levels were significantly increased. The blood glucose levels were significantly decreased for , (aqueous) ethanolic extract of *Averrhoa carambola* 200 & 400 mg/kg (116.03±2.37↓& 89.04±0.43↓) ↓), (P<0.001) **& (P<0.0001) ** when compared to control and positive control at 1hour and each and every ½ hour blood glucose levels(200 mg/kg : (P<0.05)*, (P<0.001)**& (P<0.0001)*** were changes in the dose dependent manner extract treated group of animals compared to control and positive control but 400mg/kg produce the equipotent activity

7. SUMMARY

The leaf extraction was done by sequential extraction method the leaves *of Averrhoa carambola* using the solvent with increasing polarity order (petroleum ether, ethyl acetate and ethanol) and the active extract was tested by *in vitro* & *in vivo* antidiabetic screening method. The *in vitro* antidiabetic studies have been performed based on the α-amylase inhibition assay. Each extracts were tested for α-amylase inhibition and the extract with minimum IC_{50} has been undergone phyto chemical screening. The procedure was followed by OECD maximum safe dose (2000mg/kg) were selected for further study. Finally the *invivo* antidiabetic activity of Ethanolic extract of *Averrhoa carambola* leaf was tested by using Streptozotocin induced diabetic rat. Acute toxicity study was carried out in rats. Fasting blood sample were drawn from retino orbital puncture of rats at weekly intervals till the end of the study 1,7 and 14 days. On these days fasting blood glucose were collected and analysed for glucose. At the end of the study (14^{th} day) the ethanolic extract of *Averrhoa carambola* leaf (200mg/kg p.o and 400 mg/kg p.o) treated diabetic groups showed statistically significant decrease in blood glucose similar to the standard drug glibenclamide (2mg/kg), which indicated block the alfa amyalase activity and antagonize the Streptozotocin action.The present study suggested that the isolation of active constituents from ethanolic extract of *Averrhoa carambola* leaf and characterize the compounds by using preliminary phytochemical studies.

8. CONCLUSION

In this current study, antidiabetic activity of both *in vitro* and *in vivo* has been studied for the *Averrhoa carambola* leaves, the ethanolic of higher concentration has shown the increased activity as compared with the standard drug and the control. Hence, the leaves of *Averrhoa carambola* has got the potential hypoglycaemic activity and can be safely used in diabetes induced animal model and it is less toxic even at higher concentration. Hence the glucose lowering activity of this *Averrhoa carambola* may be utilized for the treatment of type II diabetes mellitus.

9. REFERENCES

1. Agra Mf, Silva Kn, Basílio Ijld, França Pf, Barbosa-Filhojm 2008. Survey of medicinal plants used in the region northeast of brazil. *Rev bras farmacogn 18*:472-508.
2. Araújo Dam, Mafra Ra, Rodrigues Alp, Miguel-Silva V, Beirão Psl, Almeida Rn, Quintans Jr L, Souza Mfv, Cruz Js 2003. N-salicyloyltryptamine, a new anticonvulsant drug, acts on voltage-dependent na^{+}, ca^{2+}, and k^{+} ion channels. *Brit j pharmacol 140*:1331-1339.
3. Bezanilla f, armstrong cm 1977. Inactivation of the sodium channel. I. Sodium current experiments. *J gen physiol 70*:549-566.
4. Böhm M, Burmann H, Meyer W, Nose M, Schmitz W, Scholz H 1985. Positive inotropic effect of bay k 8644:camp independence and lack of inhibitory effect of adenosine. *N-s arch pharmacol 329*:447-450.
5. Chang Jm, Hwang Sj, Kuo Ht, Tsai Jc, Guh Jy, Chen Hc,Tsai Jh, Lai Yh 2000. Fatal outcome after ingestionof star fruit (*averrhoa carambola*) in uremic patients.*am j kidney dis 35*:189-193chang c-h, yeh j-h 2004. Non-convulsive status epilepticusand consciousness disturbance after star fruit (*averrhoa carambola*) ingestion in a dialysis patient.*nephrology 9*:362-365.
6. Dorigo P, Gaion Rm, Bergamin M, Giacometti A, Valentinie, Moragno I 1990. Comparison between the cardiaceffects induced by muzolimine and furosemide inguinea-pig atria. *Cardiovasc drugs ther 4*:1477-1486.
7. Fassina G, biasi M, ragazzi E, caparrotta l 1991. Adenosine:a natural modulator of l-type calcium channels inatrial myocardium? *Pharmacol res 23*:319-326.
8. Aktiviti Antioksida Dan Komponen Bioaktif Esktrak Buah Oxalidaceae 2014. Antioxidant activity and bioactive components of oxalidaceae fruit extracts. The malaysian journal of analytical sciences, vol 18 no 1 : 116 – 126.
9. Yin Sze Lim and Shi ting lee 2013. In vitro antioxidant capacities of star fruit (averrhoa carambola), an underutilised tropical fruit. Journal of biology , 1(1): 21-24.

10. Thomas R, Jebin N, Saha R, Sarma Dk 2016. antioxidant and antimicrobial effects of kordoi (*averrhoa carambola)* fruit juice and bamboo *(bambusa polymorpha*) shoot extract in pork nuggets. Food chem. 2016 jan 1;190:41-49.
11. Rupal a. Vasant and a. V. R. L. Narasimhacharya 2014. Antidotal activity of *averrhoa carambola* (star fruit) on fluoride induced toxicity in ratsinterdiscip toxicol. 2014 jun; 7(2): 103–110.
12. Phukan S And Ahmed A : evaluation of the antimicrobial, analgesic and antioxidant activity of ethanolic extract of the leaves of *averrhoa carambola*. Int j pharmscires ; 7(4): 1716-23.doi: 10.13040/ijpsr.0975-8232.7(4).1716-23.
13. Sindhu Nettem, Chinna Eswaraiah M, Dipankar B 2013. evaluation of *in-vitro* antioxidant activity of *averrhoa carambola* stem ethanolic extract . International journal of pharmtech research, 5(4):11-1618.
14. Edilene b. Ferreira, luiz claudio fernandes, sharize b. Galende, Diogenes A. G. Cortez, roberto B 2008. Bazotte, hypoglycemic effect of the hydroalcoholic extract of leaves of *averrhoa carambola l.* (oxalidaceae). Rev. Bras. Farmacogn.3(4):15-18.
15. Shejuty Shahreen, Joyanta Banik, Abdul Hafiz, Shahnaz Rahman 2012. Antihyperglycemic activities of leaves of three edible fruit plants (*Averrhoa Carambola, Ficus Hispida* and *Syzygium Samarangense*) of bangladesh. Afr J tradit Complement altern Med. 9(2): 287–291.
16. P. Dasgupta, p. Chakraborty, n. N. Bala 2013. *averrhoa carambola*: An updated review. International journal of pharma research & review, ; 2(7):54-63
17. Sultan Ayesh Mohammed, Amirin , Kooi-Yeong & Vikneswaran 2013, star fruit (Averrhoa carambola L.): From traditional uses to pharmacological activities. Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas 12 (3): 209 – 219.
18. S Shahreen, J Banik, A Hafiz, S Rahman, AT Zaman, A Shoyeb, MH Chowdhury, M Rahmatullah 2012. antihyperglycemic Activities of Leaves of Three Edible Fruit Plants (*Averrhoa carambola, Ficus hispida and Syzygium samarangense*) of

Bangladesh. African Journal of Traditional, Complementary and Alternative Medicines. 9(2):15-22

19. Daniela almeida et al.,2011 analysis of the potential Topical Anti-Inflammatory Activity of Averrhoa carambola L. in Mice. Evidence-Based Complementary and Alternative Medicine, 2(1):1-7.
20. Sandipan Mazumder , Shuvasish Choudhury 2013, leaf extract Of *Averrhoa Carambola L.* Confines The Oxidative Stress and Confers Hepatoprotection In Albino Mice. Indo American Journal of Pharmaceutical Research, 3(10):8388-8393.
21. Tanzir Hossain , Apurba Kumar Barman, Utpal Kumar Karmakar , Bishwajit Bokshi, Shrabanti Dev , Nripendra Nath biswas.phytochemical and pharmacological evaluation of leaves of *averrhoa carambola linn*. (family: oxalidaceae). Biosci bioeng commun. 3(1): 144-151
22. Ritu Singh, Jyoti Sharma, And P. K. Goyal 2014. Prophylactic role of *averrhoa carambola* (star fruit) extract against chemically induced hepatocellular carcinoma in swiss albino mice. Adv pcological sci, 1(4):55-67
23. .
24. Hamill Op, Marty A, Neher E, Sakmann B, Sigworth Fj 1981.improved patch-clamp techniques for high-resolutioncurrent recording from cells and cell-free membranepatches. *Pflügers arch 391*:85-100.
25. Martin Lc, Caramori JST, Barreti P, Soares Va 1993. Soluço intratável desencadeado por ingestão de carambola("*averrhoa carambola*") em portadores de insuficiência renal crônica. *J braz nefrol 15*:92-94.
26. Muir Ck, Lam Ck 1980. Depressant action of *averrhoa carambola* l. *Med j malaysia 34*:279-280.
27. Näbauer m, Brown l, Edmann e 1988. Positive inotropiceffects of the calcium channel activator bay k 8644 on guinea-pig and human isolated myocardium. *N-s arch pharmacol 337*:85-92.
28. Neto Mm, Costa Ja, Garcia-Cairasco N, Netto Jc, Nakagawab, Dantas M 2003. Intoxication by star fruit (*averrhoa carambola*) in 32 uraemic patients: treatment and outcome. *Nephrol dial transplant 18*:120-125.

29. Oliveira VPV, Cavalcanti FS, Bezerra CLF, Pinto jl 1989. Plantas medicinais: considerações ecológicas e usopopular. *Salusvita 8*:49-58.
30. Pio-Correa M 1931. *Dicionário de plantas úteis do brasil*. Ministério da agricultura, brasil.
31. Simasko SM, Weiland GA, Oswald RE 1988. Pharmacologicalcharacterization of two calcium currents in gh3 cells. *Am j physiol endocrinol metab 254*:e328-e336.
32. Tsai M-H, Chang W-N, Lui C-C, Chung K-J, Hsu K-T, Huangc-R, Lu C-H, Chuang Y-C 2005. Status epilepticusinduced by star fruit intoxication in patients withchronic renal disease. *Seizure 14*:521-525.
33. Tse K-C, Yip P-S, Lam M-F, Choy B-Y, Li F-K, Lui S-L, Low-K, Chan T-M, Lai K-N 2003. Star fruit intoxication in uraemic patients: case series and review of theliterature. *Int med j 33*:314-316.
34. Vasconcelos CML, Araújo MS, Silva BA, Conde-garcia EA 2005. Negative inotropic and chronotropic effectson the guinea pig atrium of extracts obtained from*averrhoa carambola* l. Leaves. *Braz j med biol res 38*:1113-1122.
35. Vasconcelos Cml, Araújo Ms, Conde-Garcia Ea 2006.electrophysiological effects of the aqueous extractof *averrhoa carambola* l. Leaves on the guinea pigheart. *Phytomedicine 13*:501-508.
36. Wang Y-C L, Liu B-M, Supernaw Rb, Lu Y-H, Lee P-Y 2006.management of star fruit-induced neurotoxicityand seizures in a patient with chronic renal failure. *Pharmacotherapy 26*:143-146.
37. Suman Das 2012. Antimicrobial and antioxidant activities of green and ripe fruits of averrhoa carambola linn. And zizyphus mauritiana lam. Asian journal of pharmaceutical and clinical research, 5(3): 102-105.